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<b>(21) International Application Number:</b> PCT/JP99/03929 <b>(22) International Filing Date:</b> 22 July 1999 (22.07.99)  <b>(30) Priority Data:</b> <table border="0"><tr><td>10/208820</td><td>24 July 1998 (24.07.98)</td><td>JP</td></tr><tr><td>10/224105</td><td>7 August 1998 (07.08.98)</td><td>JP</td></tr><tr><td>10/238116</td><td>25 August 1998 (25.08.98)</td><td>JP</td></tr><tr><td>10/254736</td><td>9 September 1998 (09.09.98)</td><td>JP</td></tr><tr><td>10/275505</td><td>29 September 1998 (29.09.98)</td><td>JP</td></tr></table> <b>(71) Applicants (for all designated States except US):</b> SAGAMI CHEMICAL RESEARCH CENTER [JP/JP]; 4-1, Nishi-Ohnuma 4-chome, Sagamihara-shi, Kanagawa 229-0012 (JP). PROTEGENE INC. [JP/JP]; 2-20-3, Naka-cho, Meguro-ku, Tokyo 153-0065 (JP).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> KATO, Seishi [JP/JP]; 3-46-50, Wakamatsu, Sagamihara-shi, Kanagawa 229-0014 (JP). KIMURA, Tomoko [JP/JP]; 302, 4-1-28, Nishiikuta, Tama-ku, Kawasaki-shi, Kanagawa 214-0037 (JP).		10/208820	24 July 1998 (24.07.98)	JP	10/224105	7 August 1998 (07.08.98)	JP	10/238116	25 August 1998 (25.08.98)	JP	10/254736	9 September 1998 (09.09.98)	JP	10/275505	29 September 1998 (29.09.98)	JP	<b>(74) Agents:</b> AOYAMA, Tamotsu et al.; Aoyama & Partners, IMP Building, 3-7, Shiromi 1-chome, Chuo-ku, Osaka-shi, Osaka 540-0001 (JP).  <b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>Without international search report and to be republished upon receipt of that report.</i>
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<b>(54) Title:</b> HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAS ENCODING THESE PROTEINS  <b>(57) Abstract</b>  The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.																	

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## DESCRIPTION

Human Proteins Having Hydrophobic  
Domains and DNAs Encoding These Proteins

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TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies against these proteins. The human cDNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the cDNAs can be utilized as gene sources for large-scale production of the proteins encoded by these cDNAs. Cells into which these genes are introduced to express secretory proteins and membrane proteins in large amounts can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

BACKGROUND ART

Cells secrete many proteins outside the cells. These secretory proteins play important roles for the proliferation control, the differentiation induction, the material transportation, the biological protection, etc. in the cells. Different from intracellular proteins, the secretory proteins exert their actions outside the cells, whereby they can be administered in the intracorporeal manner such as the injection or the drip, so that there are

hidden potentialities as medicines. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents, etc. have been currently employed as medicines. In addition, secretory proteins other than those described above have been undergoing clinical trials to develop as pharmaceuticals. Because it has been conceived that the human cells still produce many unknown secretory proteins, availability of these secretory proteins as well as genes coding for them is expected to lead to development of novel pharmaceuticals utilizing these proteins.

On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters, etc. in the material transportation and the information transmission through the cell membrane. Examples thereof include receptors for a variety of cytokines, ion channels for the sodium ion, the potassium ion, the chloride ion, etc., transporters for saccharides and amino acids, and so on, where the genes for many of them have been cloned already. It has been clarified that abnormalities of these membrane proteins are associated with a number of hitherto-cryptogenic diseases. Therefore, discovery of a new membrane protein is anticipated to lead to elucidation of the causes of many diseases, so that isolation of a new gene coding for the membrane protein has been desired.

Heretofore, owing to difficulty in the purification from human cells, these secretory proteins and membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises introduction of a cDNA library into eucaryotic cells to express cDNAs and then screening of the cells secreting, or expressing on the surface of membrane,



the objective active protein. However, this method is applicable only to cloning of a gene for a protein with a known function.

5 In general, secretory proteins and membrane proteins possess at least one hydrophobic domain inside the proteins, wherein, after synthesis thereof in the ribosome, this domain works as a secretory signal or remains in the phospholipid membrane to be trapped in the membrane. Accordingly, the evidence of this cDNA for encoding a  
10 secretory protein and a membrane protein is provided by determination of the whole base sequence of a full-length cDNA followed by detection of highly hydrophobic domain(s) in the amino acid sequence of the protein encoded by this cDNA.

15

#### OBJECTS OF THE INVENTION

The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as  
20 well as transformed eucaryotic cells that are capable of expressing these DNAs. This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

25

#### BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01550.

Fig. 2 illustrates the hydrophobicity/hydrophilicity  
30 profile of the protein encoded by clone HP02593.

Fig. 3 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10195.

- Fig. 4 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10423.
- Fig. 5 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10506.
- Fig. 6 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10507.
- Fig. 7 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10548.
- Fig. 8 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10566.
- Fig. 9 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10567.
- Fig. 10 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10568.
- Fig. 11 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01426.
- Fig. 12 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02515.
- Fig. 13 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02575.
- Fig. 14 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10357.
- Fig. 15 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10447.
- Fig. 16 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10477.
- Fig. 17 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10513.
- Fig. 18 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10540.
- Fig. 19 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10557.

Fig. 20 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10563.

Fig. 21 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01467.

5 Fig. 22 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01956.

Fig. 23 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02545.

10 Fig. 24 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02551.

Fig. 25 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

Fig. 26 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02632.

15 Fig. 27 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10488.

Fig. 28 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10538.

20 Fig. 29 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10542.

Fig. 30 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10571.

Fig. 31 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01470.

25 Fig. 32 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02419.

Fig. 33 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

30 Fig. 34 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02695.

Fig. 35 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10031.

## SUMMARY OF THE INVENTION

- Fig. 36 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10530.
- Fig. 37 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10541.
- Fig. 38 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10550.
- Fig. 39 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10590.
- Fig. 40 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10591.
- Fig. 41 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01462.
- Fig. 42 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02485.
- Fig. 43 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02798.
- Fig. 44 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10041.
- Fig. 45 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10246.
- Fig. 46 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10392.
- Fig. 47 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10489.
- Fig. 48 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10519.
- Fig. 49 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10531.
- Fig. 50 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10574.

As the result of intensive studies, the present inventors have been successful in cloning of cDNAs coding for proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention.

5 In other words, the present invention provides human proteins having hydrophobic domains, namely proteins comprising any of the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. Moreover, the present invention provides DNAs coding

10 for the above-mentioned proteins, exemplified by cDNAs comprising any of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140, as well as expression vectors that are capable of expressing any of these DNAs by in vitro translation or in

15 eucaryotic cells and transformed eucaryotic cells that are capable of expressing these DNAs and of producing the above-mentioned proteins.

#### DETAILED DESCRIPTION OF THE INVENTION

20 The proteins of the present invention can be obtained, for example, by a method for isolation from human organs, cell lines, etc., a method for preparation of peptides by the chemical synthesis, or a method for production with the recombinant DNA technology using the DNAs coding for the

25 hydrophobic domains of the present invention, among which the method for production with the recombinant DNA technology is employed preferably. For instance, in vitro expression of the proteins can be achieved by preparation of an RNA by in vitro transcription from a vector having one of

30 the cDNAs of the present invention, followed by in vitro translation using this RNA as a template. Also, introduction of the translated region into a suitable expression vector

5 by the method known in the art leads to expression of a large amount of the encoded protein in prokaryotic cells such as *Escherichia coli*, *Bacillus subtilis*, etc., and eucaryotic cells such as yeasts, insect cells, mammalian cells, etc.

10 In the case where one of the proteins of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro, when the translated region of this cDNA is introduced into a vector having an RNA polymerase promoter, followed by addition of the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, containing an RNA polymerase corresponding to the promoter. RNA polymerase promoters are exemplified by T7, T3, SP6, and the like. The vectors containing these RNA polymerase promoters are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II, and so on. Furthermore, the protein of the present invention can be expressed as the secreted form or the form incorporated into the microsome membrane, when a canine pancreas microsome or the like is added to the reaction system.

25 In the case where one of the protein of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli* etc., a recombinant expression vector bearing the translated region of the cDNA of the present invention is constructed in an expression vector having an origin which can be replicated in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator etc. and, after transformation of the host cells with this expression vector, the resulting transformant is incubated, whereby the protein encoded by said cDNA can be produced on a large scale in the

microorganism. In this case, a protein fragment containing any region can be obtained by carrying out the expression with inserting an initiation codon and a termination codon in front of and behind the selected translated region.

5 Alternatively, a fusion protein with another protein can be expressed. Only the portion of the protein encoded by this cDNA can be obtained by cleavage of this fusion protein with a suitable protease. The expression vector for *Escherichia coli* is exemplified by the pUC series, pBluescript II, the

10 pET expression system, the pGEX expression system, and so on.

In the case where one of the proteins of the present invention is produced by expressing the DNA in eucaryotic cells, the protein of the present invention can be produced as a secretory protein or as a membrane protein on the cell-

15 membrane surface, when the translated region of this cDNA is introduced into an expression vector for eucaryotic cells that has a promoter, a splicing region, a poly(A) addition site, etc., followed by introduction into the eucaryotic cells. The expression vector is exemplified by pKA1,

20 pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, and so on. Examples of eucaryotic cells to be used in general include mammalian cultured cells such as simian kidney cells COS7, Chinese hamster ovary cells CHO, etc., budding yeasts, fission yeasts, silkworm cells,

25 *Xenopus* oocytes, and so on, but any eucaryotic cells may be used, provided that they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eucaryotic cells by methods known in the art such as the electroporation method, the calcium

30 phosphate method, the liposome method, the DEAE-dextran method, and so on.

After one of the proteins of the present invention is

expressed in prokaryotic cells or eucaryotic cells, the objective protein can be isolated from the culture and purified by a combination of separation procedures known in the art. Such examples include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or solvent precipitation, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, reverse hydrophobic chromatography, affinity chromatography, and so on.

The proteins of the present invention include peptide fragments (5 amino acid residues or more) containing any partial amino acid sequence in the amino acid sequences represented by SEQ ID Nos. 1. to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Hereupon, among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins, after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP 8-187100 A]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secretory forms. Such proteins or peptides in the secretory forms shall come within the scope of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences, expression in appropriate eucaryotic cells affords proteins to which sugar chains are attached. Accordingly, such proteins or peptides to which sugar chains are attached shall come within the



scope of the present invention.

The DNAs of the present invention include all the DNAs coding for the above-mentioned proteins. These DNAs can be obtained by using a method by chemical synthesis, a method  
5 by cDNA cloning, and so on.

The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. These cDNAs are synthesized by using as templates poly(A)<sup>+</sup> RNAs extracted from human cells. The human cells may be  
10 cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and  
15 Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available, human cDNA libraries can  
20 be utilized. Cloning of the cDNAs of the present invention from the cDNA libraries can be carried out by synthesis of an oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention, followed by screening using this oligonucleotide as the probe according  
25 to the colony or plaque hybridization by a method known in the art. In addition, the cDNA fragments of the present invention can be prepared by synthesis of oligonucleotides which hybridize with both termini of the objective cDNA fragment, followed by the usage of these oligonucleotides as  
30 the primers for the RT-PCR method using an mRNA isolated from human cells.

The cDNAs of the present invention are characterized by

comprising either of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Table 1 summarizes the clone number (HP number), the cells from which the cDNA was obtained, the total base number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

SEQ ID No.	HP number	Cells	Base number	Number of amino acid residues
1, 11, 21	HP01550	Stomach cancer	510	125
2, 12, 22	HP02593	Saos-2	697	131
3, 13, 23	HP10195	HT-1080	1619	242
4, 14, 24	HP10423	U-2 OS	1066	264
5, 15, 25	HP10506	Stomach cancer	618	112
6, 16, 26	HP10507	Stomach cancer	1021	146
7, 17, 27	HP10548	Stomach cancer	1432	344
8, 18, 28	HP10566	Stomach cancer	601	97
9, 19, 29	HP10567	Stomach cancer	585	124
10, 20, 30	HP10568	Stomach cancer	1100	327
31, 41, 51	HP01426	Stomach cancer	1065	313
32, 42, 52	HP02515	Saos-2	937	229
33, 43, 53	HP02575	Saos-2	1678	467
34, 44, 54	HP10357	Stomach cancer	467	99
35, 45, 55	HP10447	Liver	875	189
36, 46, 56	HP10477	Liver	1256	363
37, 47, 57	HP10513	Stomach cancer	884	249
38, 48, 58	HP10540	Saos-2	589	98
39, 49, 59	HP10557	Stomach cancer	673	172
40, 50, 60	HP10563	Saos-2	1425	120
61, 71, 81	HP01467	HT-1080	1436	307
62, 72, 82	HP01956	Liver	997	183
63, 73, 83	HP02545	Saos-2	1753	327
64, 74, 84	HP02551	Saos-2	1117	223
65, 75, 85	HP02631	Saos-2	1380	48
66, 76, 86	HP02632	HT-1080	1503	371
67, 77, 87	HP10488	Liver	733	90
68, 78, 88	HP10538	Saos-2	3768	499
69, 79, 89	HP10542	Stomach cancer	770	106
70, 80, 90	HP10571	Stomach cancer	1229	152

91, 101, 111	HP01470	Stomach cancer	1619	358
92, 102, 112	HP02419	Stomach cancer	2054	226
93, 103, 113	HP02631	Saos-2	1380	195
94, 104, 114	HP02695	Stomach cancer	1292	339
95, 105, 115	HP10031	Saos-2	2168	487
96, 106, 116	HP10530	Saos-2	1357	393
97, 107, 117	HP10541	Stomach cancer	711	196
98, 108, 118	HP10550	Stomach cancer	651	107
99, 109, 119	HP10590	HT-1080	1310	350
100, 110, 120	HP10591	HT-1080	1400	107
121, 131, 141	HP01462	HT-1080	2050	483
122, 132, 142	HP02485	Stomach cancer	2746	334
123, 133, 143	HP02798	HT-1080	1136	267
124, 134, 144	HP10041	Saos-2	619	106
125, 135, 145	HP10246	KB	864	224
126, 136, 146	HP10392	U-2 OS	1527	258
127, 137, 147	HP10489	Stomach cancer	659	110
128, 138, 148	HP10519	Stomach cancer	710	91
129, 139, 149	HP10531	Saos-2	2182	344
130, 140, 150	HP10574	Stomach cancer	2773	428

Hereupon, the same clones as the cDNAs of the present invention can be easily obtained by screening of the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention by the use of an oligonucleotide probe synthesized on the basis of the cDNA base sequence described in any of SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and 131 to 150.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are inserted, deleted and/or substituted with other nucleotides in SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and

131 to 150 shall come within the scope of the present invention.

In a similar manner, any protein in which one or plural amino acids are inserted, deleted and/or substituted with other amino acids shall come within the scope of the present invention, as far as the protein possesses the activity of any protein having the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

The cDNAs of the present invention include cDNA fragments (10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or in the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Also, DNA fragments consisting of a sense strand and an anti-sense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

#### Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant

protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyu et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine

levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be

administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation

Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BAF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Krusbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnoli et al., J. Immunol. 145:1706-1712, 1990; Bertagnoli et al., Cellular



Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of  
5 spleen cells, lymph node cells or thymocytes include,  
without limitation, those described in: Polyclonal T cell  
stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current  
Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp.  
3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and  
10 Measurement of mouse and human Interferon  $\gamma$ , Schreiber, R.D.  
In Current Protocols in Immunology. J.E.e.a. Coligan eds.  
Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of  
hematopoietic and lymphopoietic cells include, without  
15 limitation, those described in: Measurement of Human and  
Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis,  
L.S. and Lipsky, P.E. In Current Protocols in Immunology.  
J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and  
Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-  
20 1211, 1991; Moreau et al., Nature 336:690-692, 1988;  
Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-  
2938, 1983; Measurement of mouse and human interleukin 6-  
Nordan, R. In Current Protocols in Immunology. J.E.e.a.  
Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons,  
25 Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A.  
83:1857-1861, 1986; Measurement of human Interleukin 11 -  
Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J.  
In Current Protocols in Immunology. J.E.e.a. Coligan eds.  
Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991;  
30 Measurement of mouse and human Interleukin 9 - Ciarletta, A.,  
Giannotti, J., Clark, S.C. and Turner, K.J. In Current  
Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp.

6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current protocols in Immunology, Ed by J. E. Coligan, A.M. Krusbeek, D.H. Margulies, E.M. Shevach, W Strobe, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse lymphocyte function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

#### Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit

immune stimulating or immune suppressing activity, including

without limitation the activities for which assays are

described herein. A protein may be useful in the treatment

of various immune deficiencies and disorders (including

severe combined immunodeficiency (SCID)), e.g., in

regulating (up or down) growth and proliferation of T and/or

B lymphocytes, as well as affecting the cytolytic activity

of NK cells and other cell populations. These immune

deficiencies may be genetic or be caused by viral (e.g.,

HIV) as well as bacterial or fungal infections, or may result

from autoimmune disorders. More specifically, infectious

diseases caused by viral, bacterial, fungal or other

infection may be treatable using a protein of the present

invention, including infections by HIV, hepatitis viruses,

herpesviruses, mycobacteria, Leishmania spp., malaria spp.

and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

5        Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune  
10        thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly  
15        allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

      Using the proteins of the invention it may also be  
20        possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by  
25        suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing  
30        non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent

has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD).

For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation.

Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this manner prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or

tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

5 The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in 10 Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be 15 used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T 20 cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block 25 costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce 30 antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating

autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythematosus in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

10 Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

20 Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the

transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

5 In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can  
10 be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or  
15 in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell.  
20 Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary  
25 costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected  
30 with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain protein and  $\beta$  microglobulin protein or an MHC class

II chain protein and an MHC class II protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Krusbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmant et al., J.



Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

5 Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In  
10 vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly  
15 Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse  
20 Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify,  
25 among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079,  
30 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965,

1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhargava et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

5 Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zama et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

15 Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad. Sci. USA 88:7548-7551, 1991.

#### Hematopoiesis Regulating Activity

25 A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to

stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) 5 useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as 10 thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic 15 utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or 20 ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among 25 other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence 30 embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and

- Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.
- Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylocellulose colony forming assays, R.I. Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNeice, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooner, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.
- Tissue Growth Activity
- A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.
- A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is

not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and

in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head

trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

5 Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

10 It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including  
15 vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

20 A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful  
25 for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

30 Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon);

International Patent Publication No. W095/05846 (nerve, neuronal); International Patent Publication No. W091/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

#### Activin/Inhibin Activity

10 A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among



other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., *Endocrinology* 91:562-572, 1972; Ling et al., *Nature* 321:779-782, 1986; 5 Vale et al., *Nature* 321:776-779, 1986; Mason et al., *Nature* 318:659-663, 1985; Forage et al., *Proc. Natl. Acad. Sci. USA* 83:3091-3095, 1986.

#### Chemotactic/Chemokinetic Activity

10 A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a 15 desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or 20 neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or 25 indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing 30 such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Krusbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke)).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include,

without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

#### Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22),

Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987;  
 Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein  
 et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et  
 al., J. Immunol. Methods 175:59-68, 1994; Stitt et al.,  
 Cell 80:661-670, 1995.

#### Anti-Inflammatory Activity

Proteins of the present invention may also exhibit  
 anti-inflammatory activity. The anti-inflammatory activity  
 may be achieved by providing a stimulus to cells involved in  
 the inflammatory response, by inhibiting or promoting cell-  
 cell interactions (such as, for example, cell adhesion), by  
 inhibiting or promoting chemotaxis of cells involved in the  
 inflammatory process, inhibiting or promoting cell  
 extravasation, or by stimulating or suppressing production  
 of other factors which more directly inhibit or promote an  
 inflammatory response. Proteins exhibiting such activities  
 can be used to treat inflammatory conditions including  
 chronic or acute conditions), including without limitation  
 inflammation associated with infection (such as septic shock,  
 sepsis or systemic inflammatory response syndrome (SIRS)),  
 ischemia-reperfusion injury, endotoxin lethality, arthritis,  
 complement-mediated hyperacute rejection, nephritis,  
 cytokine or chemokine-induced lung injury, inflammatory  
 bowel disease, Crohn's disease or resulting from over  
 production of cytokines such as TNF or IL-1. Proteins of the  
 invention may also be useful to treat anaphylaxis and  
 hypersensitivity to an antigenic substance or material.

#### Tumor Inhibition Activity

In addition to the activities described above for  
 immunological treatment or prevention of tumors, a protein  
 of the invention may exhibit other anti-tumor activities. A

protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues  
5 necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

10       Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria,  
15 viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast  
20 augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid,  
25 protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and  
30 violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of

embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

5 The present invention is specifically illustrated in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic operations with regard to the recombinant DNA and the enzymatic reactions were carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the manufacturer's instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

(1) Selection of cDNAs Encoding Proteins Having Hydrophobic domains

The cDNA library of fibrosarcoma cell line HT-1080 (WO98/11217), the cDNA library of osteosarcoma cell line Saos-2 (WO97/33993), the cDNA library of osteosarcoma cell line U-2 OS (WO98/21328), the cDNA library of epidermoid

carcinoma cell line KB (WO98/11217), the cDNA library of tissues of stomach cancer delivered by the operation (WO98/21328), the cDNA library of liver tissue delivered by the operation (WO98/21328), and were used for the cDNA  
5 libraries. Full-length cDNA clones were selected from respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for  
10 the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. Any clone that has a hydrophobic region  
15 being putative as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

#### (2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present  
20 invention was used for in vitro transcription/translation with a T<sub>N</sub>T rabbit reticulocyte lysate kit (Promega). In this case, [<sup>35</sup>S]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit.  
25 Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25  $\mu$ l containing 12.5  $\mu$ l  $\mu$  of T<sub>N</sub>T rabbit reticulocyte lysate, 0.5  $\mu$ l of a buffer solution (attached to the kit), 2  $\mu$ l of an amino acid mixture (without  
30 methionine), 2  $\mu$ l of [<sup>35</sup>S]methionine (Amersham) (0.37 MBq/ $\mu$ l), 0.5  $\mu$ l of T7 RNA polymerase, and 20 U of RNasin. Also, an experiment in the presence of a membrane system was carried

out by adding to this reaction system 2.5  $\mu$ l of a canine pancreas microsomal fraction (Promega). To 3  $\mu$ l of the resulting reaction solution was added 2  $\mu$ l of the SDS sampling buffer (125 mM Tris-hydrochloric acid buffer, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of the translation product was determined by carrying out the autoradiography.

10 out the autoradiography.

(3) Expression by COS7

*Escherichia coli* cells bearing the expression vector for the protein of the present invention was incubated at 37°C for 2 hours in 2 ml of the 2XYT culture medium containing 100  $\mu$ g/ml of ampicillin, the helper phage M13KO7 (50  $\mu$ l) was added, and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100  $\mu$ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TR).

20 The cultured cells derived from simian kidney, COS7, were incubated at 37°C in the presence of 5% CO<sub>2</sub> in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% fetal calf serum. Into a 6-well plate (Nunc, well diameter: 3 cm) were inoculated with  $1 \times 10^5$  COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO<sub>2</sub>. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDMEM). To the resulting cells was added a suspension of 1  $\mu$ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3  $\mu$ l of



TRANSFECTAM™ (IBF) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO<sub>2</sub>. After the sample solution was removed, the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO<sub>2</sub>. After the culture medium was replaced by a culture medium containing [<sup>35</sup>S]cystine or [<sup>35</sup>S]methionine, the incubation was carried out for one hour. After the culture medium and the cells were separated by centrifugation, proteins in the culture medium fraction and the cell-membrane fraction were subjected to SDS-PAGE.

#### (4) Clone Examples

<HP01550> (SEQ ID Nos. 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP01550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 65-bp 5'-untranslated region, a 378-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 125 amino acid residues and there existed one putative transmembrane domain. Figure 1 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 15 kDa that was almost identical with the molecular weight of 13,825 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein F45G2.c (GenBank Accession No. Z93382). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C.

5 elegans hypothetical protein F45G2.c (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.5% in the entire region.

10	HP MAKYLAQIIIVMGVGVGRFAFARALRQEF-----AASRAAADARGRAGHRSAAASNL.S- ..... ..
	CE MPWRTALKVLAAGFAVAKALTRAADVDEIKQTQQAARHAASGTQSSASETRENANSNAKL HP GLSLQEAQIILNV-SKLSPEEFVQKNYEHLFKVNDKSVGGSFYLIQSKVVRAKKERLDPEL-K ..... CE GISLEESLQIILNVKTPILNREEVEVEKHYEHLFNINDKSKGGTLLYLQSKVFRAKERIDEEFGR HP IQAQEDREKGMPHHT *.....*
15	CE IELKEEKKKKKEENAKTE

Table 2

20 Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA338859) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30 <HP02593> (SEQ ID Nos. 2, 12, and 22)  
Determination of the whole base sequence of the cDNA insert of clone HP02593 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 103-bp 5'-untranslated region, a 396-bp ORF,

and a 198-bp 3'-untranslated region. The ORF codes for a protein consisting of 131 amino acid residues and there existed four putative transmembrane domains at the C-terminus. Figure 2 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to a human OB-R gene-related protein (EMBL Accession No. Y12670). Table 3 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human OB-R gene-related protein (OB). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 67.9% in the entire region.

Table 3

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	HP	MAGIKALISLSFGGAIGLMFLMLGCALPIYNKYWPLFVLFFYILSPIPYCIARRLVDDTD
		***.***.***.***** ***** *. *****.*. *****. ***..*.*
25	OB	MAGVKALVALSFSGAIGLTFMLGCALEDYGVYWPLFVLIFHAISPIPHFIAKRVTYDSD
	HP	AMSNACKELAIFLTGTGIVVSAFGLPIVFARAHLEWGACALVLTGNTVIFATILGFFLVF
		* *.***.*** *.*****.***.***. ....*..*.*.*****.***.*** ** ****.*
	OB	ATSSACRELAYFFTTGIVVSAFGFPVILARVAVIKWGACGLVLGNAVIFLTIQGFFLIF
	HP	GSNDDFSWQQW
30		*..*****.*
	OB	GRGDDFSWEQW

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Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA306490) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

Determination of the whole base sequence of the cDNA insert of clone HP10195 obtained from cDNA library of human fibrosarcoma HT-1080 revealed the structure consisting of a 286-bp 5'-untranslated region, a 729-bp ORF, and a 604-bp 3'-untranslated region. The ORF codes for a protein consisting of 242 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was somewhat larger than the molecular weight of 27,300 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein has revealed the registration of sequences that were similar to the Aplysia VAP-33 (SWISS-PROT Accession No. P53173). Table 4 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the Aplysia VAP-33 (AP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the

5

### Table 4

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HP MAKHEQILVLDPPTDLKFKGPFDTDVVTTLNKLNRNSDRKVCVKVKTTPAPRRYCVRPNSGI  
**.* **.*...*.*****..***.**.*.....*
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10 AP MASHEQALILEPAGELRFKGPFDTVADLKLSNPTDRRICFKVKTTAPKRYCVRPNSGI

HP IDPGSTVTVSUMLQFPDYDNEKSXHKFMVQTIFAPPNTSD-MEAVWKEAKPEDELMSKL  
. \* .. \*. \*\*\*\*\* . \*\*\*\*\* . . . . \* . \*\*\* . \* . . . . \*

AP LEPKTSIAVAVMLQPFNYDPNEKNKHKFMVQSMYPADHVVESQELLWKDAPPESLMDTKL

HP RCVFEMPENNDKLNMEPSK-----AVPLNASKQDGPMKP-HSVSLNDTE

15 \*\*\*\*\* . . . . \* . . . . . \* . . . . \* . . . . \*

AP RCVFEMPDGSHQAPASDASRATDAGAHPSESALEDPTVASRKTTETQSPKRVGAVGSAGED

HP TRKLMEECKRLQGEMMKLSEENRHRLRDEGLRLRVASHD--KPGSTSTASFRDNVTSPLP  
. \*\*\* . \* \* . \* . \* . \* . . . \* . . . . . \*

AP VKKLQHCLKKAQEITSLKGENSQLKDGEIRLRKVAMTDTVSPTPLNPSPAAAAVRAFP

20 HP SLLVVIIAIFI GF FL GK FILL  
. . . \* . \*\*\* . \* . . . \*\*\* . \*

AP PVVYVVAAIILGLIGKFLL

25 Furthermore, the search of the GenBank using the base  
sequences of the present cDNA has revealed the registration  
of sequences that shared a homology of 90% or more (for  
example, Accession No. AA447905) in ESTs, but, since they  
are partial sequences, it can not be judged whether or not  
30 any of these sequences codes for the same protein as the  
protein of the present invention.

**<HP10423> (SEQ ID Nos. 4, 14, and 24)**

Determination of the whole base sequence of the cDNA insert of clone HP10423 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure consisting of a 64-bp 5'-untranslated region, a 795-bp ORF, and a 207-bp 3'-untranslated region. The ORF codes for a protein consisting of 264 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the N-terminus. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was almost identical with the molecular weight of 29,377 predicted from the ORF. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D80116) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10506> (SEQ ID Nos. 5, 15, and 25)

Determination of the whole base sequence of the cDNA insert of clone HP10506 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 53-bp 5'-untranslated region, a 339-bp ORF, and a 226-bp 3'-untranslated region. The ORF codes for a protein consisting of 112 amino acid residues and there existed one putative transmembrane domain. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,821 predicted from the ORF. When expressed in  
5 COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for  
10 example, Accession No. AA282544) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

15 <HP10507> (SEQ ID Nos. 6, 16, and 26)

Determination of the whole base sequence of the cDNA insert of clone HP10507 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 412-bp 5'-untranslated region, a 441-bp ORF, and a 168-bp 3'-  
20 untranslated region. The ORF codes for a protein consisting of 146 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-  
25 Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 16,347 predicted from the ORF.

Furthermore, the search of the GenBank using the base  
30 sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10548> (SEQ ID Nos. 7, 17, and 27)

Determination of the whole base sequence of the cDNA insert of clone HP10548 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 330-bp 5'-untranslated region, a 1035-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed four putative transmembrane domains. Figure 7 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. A143152) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10566> (SEQ ID Nos. 8, 18, and 28)

Determination of the whole base sequence of the cDNA insert of clone HP10566 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 61-bp 5'-untranslated region, a 294-bp ORF, and a 246-bp 3'-untranslated region. The ORF codes for a protein consisting of 97 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 8 depicts the



hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,452 predicted from the ORF. When expressed in COS7 cells, an expression product of about 12 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W79821) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10567> (SEQ ID Nos. 9, 19, and 29)

Determination of the whole base sequence of the cDNA insert of clone HP10567 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 77-bp 5'-untranslated region, a 375-bp ORF, and a 133-bp 3'-untranslated region. The ORF codes for a protein consisting of 124 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 9 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was almost identical with the molecular weight of 14,484 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA428475) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10568> (SEQ ID Nos. 10, 20, and 30)

Determination of the whole base sequence of the cDNA insert of clone HP10568 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 56-bp 5'-untranslated region, a 984-bp ORF, and a 60-bp 3'-untranslated region. The ORF codes for a protein consisting of 327 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36.5 kDa that was almost identical with the molecular weight of 34,326 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 40 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Leu-Thr at position 138 and Asn-Leu-Ser at position 206). Applying the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from valine at position 24. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the supernatant fraction and the membrane fraction.

30 The search of the protein data base using the amino acid sequence of the present protein has revealed that the protein was similar to the human cell-surface A33 antigen

(SWISS-PROT Accession No. Q99795). Table 5 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human cell-surface A33 antigen (A3). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.0% in the N-terminal region of 243 residues.

Table 5

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	HP	MAELPGPFLLCGALLGFLCLSGLADEVKVPTEPLSTPLGKTAELTCTYSTSVGDSFAL-EW
		*...* . *... **...*** **... .*
15	A3	MVGKMWPVLWTLCAVRVTVDASIVETPQDVLRSQGSVTLPCYHTSTSSREGLIQW
	HP	SFVQPGKPISESHPILYFTNGHLYPTGSKSKRVSLQNPPTVGVATLKLTDVHPSDTGTY
		. . . * * . * . * . * . * . * . * . * . * . *
	A3	DKLL--LHTERVVIWPFNSKN-YIHGELYKNRVSISNNAEQSDASITIDQLTMADNGTY
	HP	LCQVNNPPDFYTNGLGLINLTVLVPPSNPLCSQSGQTSVGGSTALRCSSSEGAPKPVYNW
20		* * . * . * . * . * . * . * . * . * . * . * . *
	A3	ECSVSLMSDLEGNTKSRVRLVLVPPSKPEGIEGETIIGNNIQLTCQSKESPTPQYSW
	HP	VRLGTFPTPSPGSMVQDEVSGQLILTNLSLTSSGTYRCVATNQMGASCELTLSVTEPS-
		* ... * . * . * . * . * . * . * . * . * . *
	A3	KRYNILNQEQP--LAQPASGQPVSLKNISTDTSGYYICTSSNEEGTQFCNITVAVRSPSM
25	HP	-QGRVAGALIGVLLGVLLLSVAAFCLVRFQKERGKKPKETYGGSDLREDAIAPGISEHTC
		. . * . * . * . * . *
	A3	NVALYVGIAVGVAALIIIGIIIIYCCCCRGKDDNTEDKEDARPNREAYEEPPEQLRELSR
	HP	MRADSSKGFLERPSSASTVTTTTSKLPVV
30	A3	EREEEDDYRQEEQRSTGRESPPDHLQ

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

of sequences that shared a homology of 90% or more (for example, Accession No. T24595) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01426> (SEQ ID Nos. 31, 41, and 51)

Determination of the whole base sequence of the cDNA insert of clone HP01426 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 1-bp 5'-untranslated region, a 942-bp ORF, and a 122-bp 3'-

untranslated region. The ORF codes for a protein consisting of 313 amino acid residues and there existed a putative secretory signal. Figure 11 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 34,955 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 38 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ser-Ser at position 163).

Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from tryptophan at position 17. When expressed in COS7 cells, an expression product of about 39 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the

protein was similar to the *Xenopus laevis* cortical granule lectin (EMBL Accession No. X82626). Table 6 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *X. laevis* cortical granule lectin (XL). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 67.9% in the region other than the N-terminal region.

Table 6

```

15  HP MNQLSFLLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRT
    *      **                      *      *****. . * * * . * .
XL  MLVHILLLLVTGGLSQSCEPVVIVASKNMVKQLDCDKFRSCKEIKDSNEEAQDGIYTLTS
HP  ENGVIYQTFCDMTSGGGWTLVASVHENDMRGKCTVGDWRSSQQGSKADYPEGDGNWANY
    . * . *****. *****. * *****. *****. *****
20  XL SDGISYQTFCDMTTNGGGWTLVASVHENNMAGKCTIGDRWSSQQGNRADYPEGDGNWANY
HP  NTFGSAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLG
    *****. *****. * . * . *****. * . ***** * * * . * . *
XL  NTFGSAGGATSDDYKNPGYYDIEAYNLGVWHVPNKTPLSVWRNSSLQRYRTTDGILFKHG
HP  HNLFGIYQKYPVKYGEKGCWTDNGPVI PVVYDFGDAQKTASYISPYGQREFTAGFVQFRV
    * * * . * . ***** * * . * . * . *****. * . * * * . * * * . * * *
25  XL GNLFSLYRIYPVKYIGSCSKDSGPTVPVVDLGSAKLTASFYSPDFRSQFTPGYIQFRP
HP  FNNERAANALCAGMRVTGCNTEHHCIGGGGYFPEASPQCGDFSGFDWSGYGTHVGYSSS
    . * . * * * * * . * . * * * * * * * * * * * * * * * * * . * .
XL  INTEKAALALCPGMKMECNVEHVCIGGGGYFPEADPRQCGDFAAYDFNGYGTKKFNSAG
HP  REITEAAVLLFYR
30  *****
XL  IEITEAAVLLFYL

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Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R06009) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02515> (SEQ ID Nos. 32, 42, and 52)

Determination of the whole base sequence of the cDNA insert of clone HP02515 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 176-bp 5'-untranslated region, a 690-bp ORF, and a 71-bp 3'-untranslated region. The ORF codes for a protein consisting of 229 amino acid residues and there existed a putative secretory signal at N-terminus and one putative transmembrane domain at the C-terminus. Figure 12 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was almost identical with the molecular weight of 26,000 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 25.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3',-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from phenylalanine at position 28.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human T1/ST2 receptor binding protein (Genbank Accession No. U41804). Table 7 shows the

comparison between amino acid sequences of the human protein of the present invention (HP) and the human T1/ST2 receptor binding protein (T1). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 55.8% in the entire region.

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Table 7

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15	HP MGDKIWLFPFVLLLAALPPVLLPGAAGFTPSLDSDFTFLLPAGQKECFYQPMPLKASLE *.... ** .*** . *.** . * ..*** ***.*.****. * .**** T1 MMAAGAALALALWLL--MPPVEV-GGAGPPPIQDGEFTFLLPAGRKQCFYQSAPANASLE HP IEYQVLDGAGLDIDFHLASPEGKTLVFEQRKSDGVHTVE-TEVGDMFCFDNTFSTISEK .****.*****.*** *.**.* ** * **..***** **..****.*****.***** T1 TEYQVIGGAGLDVDFTELESPQGVLLVSESRKADGVHTVEPTAAGDYKLCFDNSFSTISEK HP VIFFELILDNMGEQAQEQEDWKYITGTDILDMKLEDILESINSIKSRLSKSGHIQILLR ..*****.*.. ....* *. * . . ....*.**** **..*****.*.. .. *** T1 LVFFELIFDSL-QDDEVEGWAEAVEPEEMLDVKMEDIKESIETMRTRLERSIQMLTLRL HP AFEARDRNIQESNFDVRNFWSMVNLVVMVVSAIQVYMLKSLFEDKRKSR *****.*..*..***** **..*..*****. ....*.**** ..* T1 AFEARDRNLQEGNLERVNFWSAVNVAVLLLVAVLQVCTLKRFFQDKRPVPT
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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA381943) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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Determination of the whole base sequence of the cDNA  
 insert of clone HP02575 obtained from cDNA library of human  
 osteosarcoma cell line Saos-2 revealed the structure  
 consisting of a 55-bp 5'-untranslated region, a 1404-bp ORF,  
 and a 219-bp 3'-untranslated region. The ORF codes for a  
 protein consisting of 467 amino acid residues and there  
 existed a putative secretory signal at the N-terminus.  
 Figure 13 depicts the hydrophobicity/hydrophilicity profile,  
 obtained by the Kyte-Doolittle method, of the present  
 protein. In vitro translation resulted in formation of a  
 translation product of 52 kDa that was almost identical with  
 the molecular weight of 54,065 predicted from the ORF. In  
 this case, the addition of a microsomal led to the formation  
 of a product of 57 kDa which is considered to have a sugar  
 chain being attached after secretion. In addition, there  
 exist in the amino acid sequence of this protein three sites  
 at which N-glycosylation may occur (Asn-Arg-Thr at position  
 171, Asn-Ser-Thr at position 239 and Asn-Asp-Thr at position  
 377). Application of the (-3',-1) rule, a method for  
 predicting the cleavage site of the secretory signal  
 sequence, allows to expect that the mature protein starts  
 from histidine at position 29. When expressed in COS7 cells,  
 an expression product of about 55 kDa was observed in the  
 supernatant fraction.

The search of the protein data base using the amino  
 acid sequence of the present protein revealed that the  
 protein was similar to the human  $\alpha$ -L-fucosidase (SWISS-PROT  
 Accession No. P04066). Table 8 shows the comparison between  
 amino acid sequences of the human protein of the present  
 invention (HP) and the human  $\alpha$ -L-fucosidase (FC). Therein,



the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both  
 5 proteins shared a homology of 54.8% in the entire region.

Table 8

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	HP	MRPQELPRLAFPLLLLLLLLLLPPPPC-PAHSATRFDPTWESLDARQLPAWFDQAKFGIFI
10		.*****.* .. . *... *...* ***.*.....*****.*
	FC	MRSRPAGPALLLLLLLFLGAESVRAQPPRRYTPDWPSLDSRPLPAWFDEAKFGVFI
	HP	HWGVFSVPFSGSEWFWWYQKEKIPKYVEFMKNYPPSFKYEDFGPLFTAKFFNANQWAD
		*****.*.....** * *. * ..*****.*.*.....***
	FC	HWGVFSVPAWGSEWFWWHWQGEGRPQYQRFMRDNYPGFSYADFGPQFTARFFHPEEWAD
15	HP	IFQASGAKYIVLTSKHHEGFTLWGSEYSWNWNAIDEGPKRDIVKELEVAIRNRTDLRFGI
		***.*****.***.***** * * *****. * ***.* * ..*.*
	FC	LFQAAGAKYVVLTTKHHEGFTNWPSPVSWNWSKDVGPHRDLVGELGTALRKR-NIRYGL
	HP	YYSLEWFHPLFLEDESSSFHKRQFPVSKTLPELYELVNNYQPEVLWSDGDGGAPDQYWN
		*..*****.* *.....* ..*****.***.*.....* .. ** ***
20	FC	YHSLLEWFHPLYLLDKKNGFKTQHFSVAKTMEPLYDLVNSYKPDLIWSDGEWECPTTYWN
	HP	STGFLAWLYNESPVRGTVVTNDRWGAGSICKHGGFYTCSDRYNPGHLLPHKWENCMITDK
		**.*.*****.***..**.*.....* ..*****.*.*.....* * ***** *
	FC	STNFLSWLYNDSPVKDEVVNDRWGQNCCHGGYNCEDKFKPQSLPDHKWEMCTSIDK
	HP	LSWGYRREAGISDYLTIEELVKQLVETVSCGNLLMNIGPTLDGTISVVFEERLRQMGSW
25		*****. ....* ..*.....*.*.....* * ..***** * * ..***** ..*
	FC	FSWGYRRDMALSDVTEESEIISLVQTVSLGGNYLLNIGPTKDGLIVPIFQERLLAVGKW
	HP	LKVNGEAIYETHTRWSONDTVTPDVWYTSKPKKLVYAIFLKWPTSGQLFLGHPKAILGA
		*..*****.....* * ..*.....* .. *****.*.....* * ..* ..
	FC	LSINGEAIYASKPWRVQWEKNTTSVWYTSKGS--VYAIFLHWPENGVLNLESPITT-ST
30	HP	TEVKLLGHGQPLNWISLEQNGIMVELPQLTIHQMPCKKGWALALTNI
		*.....* *.* ..*.....* ..* ..*.....* ..*
	FC	TKITMLGIQGDLDKWDTPDKGLFISLPQLPPSAVPAEFAWTIKLTGVK

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Determination of the whole base sequence of the cDNA  
<HP10447> (SEQ ID Nos. 35, 45, and 55)

protein of the present invention.  
any of these sequences codes for the same protein as the  
are partial sequences, it can not be judged whether or not  
example, Accession No. AA477156) in ESTs, but, since they  
of sequences that shared a homology of 90% or more (for  
sequences of the present cDNA has revealed the registration  
Furthermore, the search of the Genbank using the base  
weight of 10,923 predicted from the ORF.

of 11 kDa that was almost identical with the molecular  
translation resulted in formation of a translation product  
Doolittle method, of the present protein. In vitro  
hydrophobicity/hydrophilicity profile, obtained by the Kyte-  
transmembrane domains. Figure 14 depicts the  
of 99 amino acid residues and there existed two putative  
untranslated region. The ORF codes for a protein consisting  
5'-untranslated region, a 300-bp ORF, and a 54-bp 3'-  
stomach cancer revealed the structure consisting of a 113-bp  
insert of clone HP10357 obtained from cDNA library of human  
Determination of the whole base sequence of the cDNA  
<HP10357> (SEQ ID Nos. 34, 44, and 54)

of the present invention.  
of these sequences codes for the same protein as the protein  
partial sequences, it can not be judged whether or not any  
example, Accession No. N28668) in ESTs, but, since they are  
of sequences that shared a homology of 90% or more (for  
sequences of the present cDNA has revealed the registration  
Furthermore, the search of the Genbank using the base

insert of clone HP10447 obtained from cDNA library of human liver revealed the structure consisting of a 271-bp 5'-untranslated region, a 570-bp ORF, and a 34-bp 3'-untranslated region. The ORF codes for a protein consisting of 189 amino acid residues and there existed five putative transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA296976) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10477> (SEQ ID Nos. 36, 46, and 56)

Determination of the whole base sequence of the cDNA insert of clone HP10477 obtained from cDNA library of human liver revealed the structure consisting of a 149-bp 5'-untranslated region, a 1092-bp ORF, and a 15-bp 3'-untranslated region. The ORF codes for a protein consisting of 363 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 16 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,884 predicted from the ORF.

The search of the protein data base using the amino

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

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25	<p>PG LRSNVLKGRDVGRTLSFGNQLYHLIQNWPVHYRSP</p> <p>*****</p> <p>HP LRPDYALGHRQLVTRTDCPGDALFDLLRTWPHFTATVKKPRPARSVSKRSRKEPPPRRLPA</p> <p>PG DGLVYEGRGWNFTGAHSGHILWNPMISIGISFMGNVMDRVPTPQAIRAAGLL-ACGVAQGA</p> <p>*****</p> <p>HP DGLVYEGRGWVGAHTLGH-NSRGFGVAIVGNVTAALPTFAALRTVARDTLPSCAVRAGL</p> <p>PG SECAQHLSTPLRYVVVSHT--AGSSCNTPAASCQQAARNVQHHYHMKTLGWCDVGYNFLIGE</p> <p>*****</p> <p>HP RGRPKTLQLPLGLFYVHHHTVVPAPPCDFTTRCAANMRSMQRYHQDTQGWGDIGYSFVGS</p> <p>MSRSMILAWALPSLLRLGAQAQETEDBACCSPIVPRNEMKALA-</p> <p>*****</p> <p>HP QQVWGTLVLTLQRTLEPVHLLQCMSEQQLAQVAANATKKEFTFAFLGCPAIIHPRCRWGAPAY</p> <p>HP NGALDGVILGDYLSRTPPEPRPSLSHLSQYGAAGVARDPGRSNFRQNGAALTSAISIA</p> <p>HP MVDSLAVTLAAGNLGLTFLRGSQTQSHPDLTGEGCWDQLSAPRTFTLLDPKASLLTKAFL</p>	15
20		
25		

Table 9

acid sequence of the present protein revealed that the protein was similar to the human peptidoglycan recognition protein (GenBank Accession No. AF076483). Table 9 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human peptidoglycan recognition protein (PG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 54.8% in the entire region.

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of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10513> (SEQ ID Nos. 37, 47, and 57)

Determination of the whole base sequence of the cDNA insert of clone HP10513 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 134-bp 5'-untranslated region, a 750-bp ORF, and a 0-bp 3'-untranslated region. The ORF codes for a protein consisting of 249 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 27,373 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0512 (GenBank Accession No. AB011084). Table 10 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0512 (KI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 31.6% in the C-terminal region of 196 amino acid residues.

Table 10

HP MGPGRGAGWVAAGLLTGAGACYCICYRLLTRGRRG

5

KI RGRGRRPVAMQKRPFPYRDEILGVRDLRKVLALLQKSDPFIQGVALLTLNNANYSN  
HP DRELGIRSSKSAEDLTGSDYDVLNAEQLLTLLESTEDPVIIRALITLGNMAAFSV  
\* \* \* \* \*

10

KI QETIRKLGELPIIANMINKTDPHIKKEKATAMANNLSENYENQRLQVYNNKVMDDIMASN  
HP NQAIIRLGGIPVAAKINSHSNQSIKKEKATNATNLTNVNENQIKIKVQVTKLTLNLSEN  
\* \* \* \* \*

15

KI LNSAVQVVGKFKLTNNMTTNDYQHLTVNSIANF--FRLLSQGGGKIKVEIKILSNFAEN  
HP PAMTEGLTRAQVDSSFLSYDSHVAKKEILLRVLTLFQNKCNCLKIEGHLAVQPTFTGSL  
\* \* \* \* \*  
KI PDMLKKLTLSTQVPAFSSLYNSVSEILINALTLFEIYYDNLRAE--VFNYREFNKGSL  
HP FFL-LHGECAQKIRALVDHDAEVEKKEKVVTIIPKI  
\* \* \* \* \*

KI FYLCITTSQVCVKKIRALANHHDDLVLKVKVIKLVNKF

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Furthermore, the search of the Genbank using the base  
sequences of the present cDNA has revealed the registration  
of sequences that shared a homology of 90% or more (for  
example, Accession No. N92228) in ESTs, but, since they are  
partial sequences, it can not be judged whether or not any  
of these sequences codes for the same protein as the protein  
of the present invention.

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<HP10540> (SEQ ID Nos. 38, 48, and 58)

Determination of the whole base sequence of the cDNA  
insert of clone HP10540 obtained from cDNA library of human  
osteosarcoma cell line Saos-2 revealed the structure

consisting of a 47-bp 5'-untranslated region, a 297-bp ORF, and a 245-bp 3'-untranslated region. The ORF codes for a protein consisting of 98 amino acid residues and there existed two putative transmembrane domains. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CEF49C12.12 (GenBank Accession No. Z68227). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CEF49C12.12 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 36.1% in the entire region.

Table 11

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25	HP M-ASLLCCGPKLAACGIVLSAWGVIMLIMLGIFNVHSAVLIEDVPFTEKDFENGPNQNIY
	*        *** *    * * * * *    * * * *        *
	CE MGKICPLMGPKMSAFCMVMSVWGVIFLGLLGVFFYIQAVTLFPDLHF-EGHGKVPSSVID
	HP NLYEQVSYNCFIAAGLYLLLGGFSFCQVRLNKRKEYMVR
	*        * * * * *        * *        **
30	CE AKYNEKATQCWIAAGLYAVTLIAVFWQ---NKYNTAQIF

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Furthermore, the search of the GenBank using the base  
 sequences of the present cDNA has revealed the registration  
 of sequences that shared a homology of 90% or more (for  
 example, Accession No. AA420715) in ESTs, but, since they  
 are partial sequences, it can not be judged whether or not  
 any of these sequences codes for the same protein as the  
 protein of the present invention.

Determination of the whole base sequence of the cDNA  
 insert of clone HP10557 obtained from cDNA library of human  
 stomach cancer revealed the structure consisting of a 24-bp  
 5'-untranslated region, a 519-bp ORF, and a 130-bp 3'-  
 untranslated region. The ORF codes for a protein consisting  
 of 172 amino acid residues and there existed a putative  
 secretory signal at the N-terminus. Figure 19 depicts the  
 hydrophobicity/hydrophilicity profile, obtained by the Kyte-  
 Doolittle method, of the present protein. In vitro  
 translation resulted in formation of a translation product  
 of 32 kDa that was larger than the molecular weight of  
 18,844 predicted from the ORF. In this case, the addition of  
 a microsomal led to the formation of a product of 39 kDa  
 which is considered to have been subjected to some  
 modification after secretion. In addition, there exist in  
 the amino acid sequence of this protein no site at which N-  
 glycosylation may occur. Application of the (-3',-1) rule, a  
 method for predicting the cleavage site of the secretory  
 signal sequence, allows to expect that the mature protein  
 starts from glycine at position 32. When expressed in COS7  
 cells, an expression product of about 20 kDa was observed in  
 the supernatant fraction and the membrane fraction.



The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human progesterone binding protein (EMBL Accession No. AJ002030). Table 12 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human progesterone binding protein (PG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.5% in the C-terminal region of 151 amino acid residues.

Table 12

15	HP	MVGPAP
	PG MAAGDGDVKLGTLGSGSESSNDGGSESPGDAGAAAEGGWAAAAALALLTGGGEMLLNVAL	
	HP RRRRLRPLAALALVLALAPGLPTARAGQTPRPAERGPPV--RLFTEEEELARYGGEEEDQPI	
20	PG VALVLLGAYRLWVRWGRRGLGAGAGAGEESPATSLPRMKKRDFSLEQLRQYDG-SRNPRI	** . . . . . * . . . * . * . . . *
	HP YLAVKGVVFDVTSGKEFYGRGAPYNALTGKDSTRGVAKMSLDPADLTHDTTGLTAKELEA	
	PG LLAVNGKVFVDVTGSKFYGPAGPYGIFAGRDA SRGLATFCLDKDALRDEYDDLSDLNVAQ	***. * *****. . . . . * . . . . . * . . . . . *
25	HP LDEV--FTKVYKAKYPIVGYTARRILNEDGSPNLDKPEDQPHFDIKDEF	
	PG MESVREWEMQFKEY---DYVG-RLLKPGEEPS-EYTDEEDTKDHNKQD	. . . * . . . . * . . . . * . . . . * . . . . *

30 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA101709) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10563> (SEQ ID Nos. 40, 50, and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10563 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 126-bp 5'-untranslated region, a 363-bp ORF, and a 936-bp 3'-untranslated region. The ORF codes for a protein consisting of 120 amino acid residues and there existed two putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 18.5 kDa that was larger than the molecular weight of 13,180 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein F27F23.15 (Genbank Accession No. AC003058). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the A. thaliana hypothetical protein F27F23.15 (AT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.5% in the entire region.

Table 13

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HP  MMPSRTNLATGIPSSKVYSRLSSTDGIDLQFKKTPPKIPYKAIALATVFLIGAFLI
                                     *..* .. . . . * ..*..* ..*..*..*
5  AT          MAYVDHAFSISDEDLMIGTSY-TVSNRPPVKEISLAVGLLVFGTLGI
HP  IIGSLLLLSGYISKGGADRAVPVLIIGILVFLPGFYHLRIAYYASKGYRGYSYDDIPDFDD
    ..* .. . . . * ..*..*..*..*..*..*..*..*..*..*..*..*
AT  VLGFFMAYNRVG-GDRGHGIFIVLGCLLFIPGFYYTRIAYYAYKGYKGFSSNIPSV

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA083574) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP01467> (SEQ ID Nos. 61, 71, and 81)

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Determination of the whole base sequence of the cDNA insert of clone HP01467 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 65-bp 5'-untranslated region, a 924-bp ORF, and a 447-bp 3'-untranslated region. The ORF codes for a protein consisting of 307 amino acid residues and there existed three putative transmembrane domains. Figure 21 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

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The search of the protein data base using the amino

acid sequence of the present protein revealed that the protein was similar to the rat Sec22 homologue (Genbank accession No. U42209). Table 14 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat Sec22 homologue (RN). Therein, the marks of '-', '\*' and '.' represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 94.6% in the N-terminal region of 241 amino acid residues. The protein of the present invention was longer by 53 amino acids at the C-terminus than the rat Sec22 homologue.

Table 14

15	
5	HP MSMLASAVIRVVDGLPLSASTDYEQSTGMQECRKYYFKMLSRKLAQLPDRCTLTKTGHYNI *****. RN MSMLASAVIRVVDGLPLSASTDCEQSAVGQECRKYYFKMLSRKLAQLPDRCTLTKTGRHNI HP NFISSLGVSYMMLCTENYPNVLAFFSLDELQKEFTTYYNMKNTNTAVRPYCFIEFDNIQ ***** RN NFISSLGVSYMMLCTENYPNVLAFFSLDELQKEFTTYYNMKNTNTAVRPYCFIEFDNIQ HP RTKQRYNNPRLSTKINLSDMQTEIKLRPYPYQISMCIELGSANGVTSAFSDCKGAGKISS ***** RN RTKQRYNNPRLSTKINLSDMQTEIKLRPYPYQIPMCIELGSANGVTSAFSDCKGAGKISS HP AHQRLPAPATLSGIVGFILSLCGALNTLIRGFHAIRESLLQSDGDDFNYYIIAFFLGTAACTLY *****. RN AHQRLPAPATLSGIVAFILSLCGALNTLIRGFHAIRESLLQSDGEDFSSYMI AFFLGTAACTLY HP QCYLTVYYTGWRNVKSFILTFGLICLCNMXYLETNLWOLFHFHVTVGAFVTLQIWLQQAQG * RN QMICLCLQGRKERT
20	
25	
30	

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA421925) in ESTs, but, since they  
5 are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01956> (SEQ ID Nos. 62, 72, and 82)

10 Determination of the whole base sequence of the cDNA insert of clone HP01956 obtained from cDNA library of human liver revealed the structure consisting of a 86-bp 5'-untranslated region, a 552-bp ORF, and a 359-bp 3'-untranslated region. The ORF codes for a protein consisting  
15 of 183 amino acid residues and there existed one putative transmembrane domain. Figure 22 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product  
20 of 20.5 kDa that was almost identical with the molecular weight of 20,073 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the yeast hypothetical protein 21.5  
25 kDa (SWISS-PROT Accession No. P53073). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the yeast hypothetical protein 21.5 kDa (SC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that  
30 of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

of 34.3% in the C-terminal region of 108 amino acid residues.

Table 15

5	HP	MTAÖGGGLVANNRGRFRKWAIELSGPGGSGRGRSDRGSGGDSLYPVGYLDKQVPDTS	SC	MSFEQPEYEWAKHLLDTKYLEKYNINÖNSNTLPSPPGFEENSSKGNVTRKQÖDATSQTTSLA
			HP	VÖETDRIILVEKRCWDIALGPIKQIPMNLFIMYMAGNTISIFPTMVCMMAWRPIQALMAI
			SC	ÖKNQITVLÖVÖKAWÖIALÖPAKSIPIMNIFMSYMSGTSLÖIIPIMTALMLSGPIKAIFST
10	HP	SATPK--MLESSSQKFLÖGLVYLIGNIMGLALAV-Y-KQÖSMGLPTTHASDWLAFIEPPE		.....
	SC	RSAPKPVILGNKATQÖSVÖTAMFMYIVFÖGLVMYIGYRKILNSMGLIPNAKGDWLPWERIAH		
	HP	RMEFSGGGLTL		
15		SC YNNGLÖWFSD		

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AAI59753) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02545> (SEQ ID Nos. 63, 73, and 83)  
Determination of the whole base sequence of the cDNA insert of clone HP02545 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 133-bp 5'-untranslated region, a 984-bp ORF, and a 636-bp 3'-untranslated region. The ORF codes for a

protein consisting of 327 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 23 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat embigin (EMBL Accession No. AJ009698). Table 16 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat embigin (RN). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 65.4% in the entire region.

Table 16

5	HP MRALPGLTLEARARTRPRLTLTQCLTAAAPSSADGSA PDSPTSPPLREIIMAN--NFSLE RN MRSHLTGRLATVAPGCSLTLL-YLTAATRPDRAVGDPA DSAFTSLPVRHEEMAKYANLSLE HP SHNISLTSEHSSMPVEKNITLERPSNVNLTTCQFTTSGDLNAVNTWKKGDEGLE--NNYLV RN LYNISLTLEQTRVS-EQNIITLERPSHLETCFTTATFEDVMSMNVTWKKDALTLETTDGFNT HP SATGSLTYTQYRFTIINSKQMGSSYSCFFREKEKQGRGTFFNFKVPBELHGNKPKPLISYVGDSLT RN TKMGDTLYSQYRFTVFNPKQMGKYS CFLGEE--LRGTFNIRKVPKVGKPKPLITYVGDSLT HP VLTCKCQNCFP LNWWTWSSNGSVKVPVGQ M-NKYVINGTYYANETKTKITQLTLEEDGESY RN VLTCKCQNCFP LNWWTWSSNGSNGTAVP IDVHVNDKFDINGSYANETKTKVKHLLLEEDGESY HP WCRALFQLGSESEEHIE TLVLSYLVPLKPFLLVIAFVILLVAIILCEKYTQKKKHSDEG RN WCRAAFPLGSESEEHIKITLVLSFMVPLKPFLLAIAFVILLVAIILCEVYTQKKKNPDPDG HP KFEFQIEQTKSDSDSNGIENNVPFRRKKNESLGQ RN KFEFQIEQTKSDSDSNGIENNVPFRRKKTDSGDQ
10	
15	
20	

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA312629) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02551> (SEQ ID Nos. 64, 74, and 84)  
Determination of the whole base sequence of the cDNA insert of clone HP02551 obtained from cDNA library of human



osteosarcoma cell line Saos-2 revealed the structure consisting of a 61-bp 5'-untranslated region, a 672-bp ORF, and a 384-bp 3'-untranslated region. The ORF codes for a protein consisting of 223 amino acid residues and there  
5 existed a putative secretory signal at the N-terminus. Figure 24 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was somewhat larger than  
10 the molecular weight of 24,555 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 26 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the  
15 secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 20.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse FGF binding protein  
20 (GenBank Accession No. U49641). Table 17 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse FGF binding protein (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the  
25 protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 21.2% in the entire region other than the N-terminal region. In particular, all the eight cysteine residues contained in the  
30 both proteins were conserved.

Table 17

[illegible]

20 Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA317400) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02631> (SEQ ID NOS. 65, 75, and 85)

30 Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 147-bp ORF,

and a 1191-bp 3'-untranslated region. The ORF codes for a protein consisting of 48 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa or less.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP02632> (SEQ ID Nos. 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP02632 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 50-bp 5'-untranslated region, a 1116-bp ORF, and a 337-bp 3'-untranslated region. The ORF codes for a protein consisting of 371 amino acid residues and there existed eight putative transmembrane domains. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELC2H12 (GenBank Accession No. U23169). Table 18 shows the comparison between amino acid sequences

30

of the human protein of the present invention (HP) and the C. elegans hypothetical protein CELC2H12 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 51.4% in the entire region.

Table 18

10	HP MAWTKYQLFLAGLMLVTGSLNTLSAKWADNFMAGCGGSKSEHSFQHPFLQAVGMFLGEFS CE MVAFAVVISVMVMVVTGSLNTICAKWADSIKAD-----GVFNNHHPFLQATCMFFGEFL HP CLAAYL-----LRCRAAGQSDS-----SVDPQQPFNPFLLFPALCDMTGTSL 15 CE CLVFFLLIFGYKRYVMNRANVGESGVSVEITSEKPFLLPPNPFLLFPALCDILGTSL HP NYVALNMTSASSFQMLRGAVIIFTGLSVAFLGRRLVLSQWLGIATAGLVVGLADLL 20 CE NYIGLNLTTASSFQMLRGAVIIFTGLSVGMLNNAQIKPFKWFGLFVMLGLVIVGVTDIY HP SKHDSQHKLTSEVITGDLIIIMAQIIVAIQMVLSEKPFVYKHNHPLRAVGTGLFGEVILS CE YDDPFLDBDKNAIITGNLLIWAQIIVAIQMVEYEQKYLTKYDVPALFAVGBLFGVMVTL HP LLVPMYYIPAG-SFSGNPRGTLEDALDAFCQVGQGPLIAVALTGNISSIAFFNFAGISV 25 CE ILMIPFYIYIHVPRTFTSTNPEGRLEDFVYAWKKEITTEBPITALSGTVVSIASFNFAGVSV HP TKLSATTRMVLDSLRVTVVIAWALSLALGWFAFHATQILGFLILLIGTALYNGIHRPILGR 30 CE TKLSATTRMVLDSVRITLVIWVVSIPLFHEKFIATQILSGFAMLIIGTLIYNDILIGPWER HP LSRGRPLAESESEQERTLGGTRTPINDAS CE KNILPNLSSHANCARCWLICIGGGDSELIEYEQEDQEHLMFA
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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N50907) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10488> (SEQ ID Nos. 67, 77, and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10488 obtained from cDNA library of human liver revealed the structure consisting of a 39-bp 5'-untranslated region, a 273-bp ORF, and a 421-bp 3'-untranslated region. The ORF codes for a protein consisting of 90 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,151 predicted from the ORF. When expressed in COS7 cells, an expression product of about 6 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H73534) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10538> (SEQ ID Nos. 68, 78, and 88)

Determination of the whole base sequence of the cDNA  
 insert of clone HP10538 obtained from cDNA library of human  
 osteosarcoma cell line Saos-2 revealed the structure  
 consisting of a 357-bp 5'-untranslated region, a 1500-bp ORF,  
 and a 1911-bp 3'-untranslated region. The ORF codes for a  
 protein consisting of 499 amino acid residues and there  
 existed at least four putative transmembrane domains. Figure  
 28 depicts the hydrophobicity/hydrophilicity profile,  
 obtained by the Kyte-Doolittle method, of the present  
 protein. In vitro translation resulted in formation of a  
 translation product of high molecular weight.  
 The search of the protein data base using the amino  
 acid sequence of the present protein revealed that the  
 protein was similar to the mouse pore-forming K<sup>+</sup> channel  
 subunit (Genbank Accession No. AF056492). Table 19 shows the  
 comparison between amino acid sequences of the human protein  
 of the present invention (HP) and the mouse pore-forming K<sup>+</sup>  
 channel subunit (MM). Therein, the marks of -, \*, and .  
 represent a gap, an amino acid residue identical with that  
 of the protein of the present invention, and an amino acid  
 residue similar to that of the protein of the present  
 invention, respectively. The both proteins shared a homology  
 of 32.4% in the N-terminal region of 241 amino acid residues.

Table 19

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HP  MVDRGPLLTSALFYLAIGAAIFEVLEEPHWKEAKKNYYTQKLHLLKEFPCLGQEGLDK
      * . . . . . ** . . . . . ** . . . . . * . . . . . ** . . . . .
5  MM MRSTLLALLLVLLYLVSALVFOALEQPHEQQAQKKMDHGRDQFLRDHPCVSQKSLED
HP  ILEVVSDAAGQG-----VAITGNQTFNNWNWPNAMIFAATVITTIGYGNVAPKTPAGRLE
      . . . . . * * * . . . . . ** . . . . . ** . . . . . ** . . . . .
MM  FIKLLVEALGGGANPETSWTNSSNHSSAWNLSAFFFSGTIITTIGYGNIVLHTDAGRLE
HP  CVFYGLFGVPLCLTWISALGKFFGGRAKR-----LGQFLTKRGVSLRKAQITCTVIFIVWG
10  * . . . . * . . . . . * . . . . . * . . . . . * . . . . . *
MM  CIFYALVGIPFLFGMLLAGVGDRLGSSSLRRGIGHIEAIFLKWVPPGLVRSLSAVLFLIG
HP  VLVHLVIPPFVFMVTEGWNYYIEGLYYSFITISTIGFGDFVAGVNPSANYHALYRYFVELW
      * . . . . ** * . . . . * . . . . . ** . . . . . * . . . . .
MM  CLLFVLTPFTFVSYMESWSKLEAIYFVIVTLTTVGFGDYVPG-DGTGQNSPAYQPLVWF
15  HP  IYLGLAWLSLFVNWKVSMFVEVHKAIKRRRRRRKESFESSPHSRKALQVKGSTASKDVNI
      * . . . . .
MM  ILFGLAYFASVLTTIGNWLRVSRRTTRAEMGGLTAQAASWTGTVTARVTQRTGPSAPPE

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20 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R25184) in ESTs, but, since they are partial sequences, it can not be judged whether or not any

25 of these sequences codes for the same protein as the protein of the present invention.

<HP10542> (SEQ ID Nos. 69, 79, and 89)

30 Determination of the whole base sequence of the cDNA insert of clone HP10542 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 23-bp 5'-untranslated region, a 321-bp ORF, and a 426-bp 3'-

5 untranslating region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 29 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,724 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

10 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA029683) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

20 Determination of the whole base sequence of the cDNA insert of clone HP10571 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 95-bp 5'-untranslating region, a 459-bp ORF, and a 675-bp 3'-untranslating region. The ORF codes for a protein consisting of 152 amino acid residues and there existed one putative transmembrane domain. Figure 30 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20 kDa that was larger than the molecular weight of 17,062 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 23 kDa



which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ile-Thr at position 10).

5 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA105822) in ESTs, but, since they are partial sequences, it can not be judged whether or not  
10 any of these sequences codes for the same protein as the protein of the present invention.

<HP01470> (SEQ ID Nos. 91, 101, and 111)

Determination of the whole base sequence of the cDNA  
15 insert of clone HP01470 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 157-bp 5'-untranslated region, a 1077-bp ORF, and a 385-bp 3'-untranslated region. The ORF codes for a protein consisting of 358 amino acid residues and there existed one putative  
20 transmembrane domain. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 43 kDa that was somewhat larger than the molecular weight  
25 of 40,489 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa from which the secretory signal is considered to have been cleaved and a product of 43.5 kDa which is considered to have been subjected to some modification. Application of the  
30 (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 23. When

expressed in COS7 cells, an expression product of about 44 kDa was observed in the supernatant fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Caenorhabditis elegans

hypothetical protein 39.9 kDa (SWISS-PROT Accession No. Q10005). Table 20 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C. elegans hypothetical protein 39.9 kDa (CE).

Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 58.9% in the entire region.

Table 20

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HP MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRASIKDIKKAYRKLALQLHPDRNPDD  
 \*.. \* \*\*\*\*\*...\*. ..\*\*\*\*\* .\*\*\*\*\*..\*\*

5 CE MRILNVSLVLAASSLVAFVECGRDFYKILGVAKNANANQIKKAYRKLAKELHPDRNQDD  
 HP PQAQEKFDLGAAYEVLSDSEKRKQYDITYGEEGL--KDGHQSSHGDIFSHFFGDFGFMFG  
 \*.\*\*\*\*\*.\*\*\*\*\*.\*\*\* \*\* .\*\*\*\*. ...\* .. \* \* \* \* \* \* \* \*

CE EMANEKFDLSSAYEVLSDKEKRAMYDRHGEEGVAKMGGGGGGGHDPFSSFFGDF-FG-G  
 HP GTPRQQRNIPRGSDIIVDLEVTLEEYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTT  
 10 \*. . . . .\*. . . . . \* \* \* \* \* . \* . \* . \* . . . . \* \* \* \* \* .

CE GGGHGGEETPKGADVITIDLFVTLEEYNGHFVEIKRKKAVYKQTSQTRQCNCRHEMRTE  
 HP QLGPGRFQMTQEVVCECPNVKLVNEERTLEVEIEPGVRDGMETPFGEPEPHVDGEPGD  
 \*.\*\*\*\*\* \* \* \* \* \* \* \* \* \* \* . \* . . . \* \* \* \* \* . \* . . . .

CE QMGQGRFQMFQVKVCDECPNVKLVQENKVLVEVEVEVGADNGHQQIFHGEGEPHIEGDPGD  
 15 HP LRFRIKVVVKHPIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVVHISRDKITRPGAK  
 \*. . . . \* \* \* \* \* \* \* \* \* \* \* \* . \* \* \* \* . \* \* \* \* \* \* . \* \* \* \* .

CE LKFKIRIQKHPRFERKGDDLYTNVTISLQDALNGFEMEIQHLDGHIVKVQDKVTWPGAR  
 HP LWKKGEGLPNFDNNNIKGSIIITFDVDFPKEQLTEEAREGIKQLLKQGSVQ-KVYNGLQG  
 \*. . . . . \* \* \* \* \* . \* \* \* \* . \* \* \* \* . \* \* \* \* . \* \* \* \* .

20 CE LRKKDEGMPSLDNNKKGMLVVTDFVEFPKTELSDEQKAQIIEILQQNTVKPKAYNGL

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282838) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30 <HP002419> (SEQ ID Nos. 92, 102, and 112)

Determination of the whole base sequence of the cDNA insert of clone HP02419 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 253-bp

5'-untranslated region, a 681-bp ORF, and a 1120-bp 3'-untranslated region. The ORF codes for a protein consisting of 226 amino acid residues and there existed four putative transmembrane domains. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0108 (SWISS-PROT Accession No. Q15012). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0108 (KI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 43.9% in the entire region.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA173214) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 588-bp ORF, and a 750-bp 3'-untranslated region. Although the 49th amino acid residue is encoded by a stop codon, it is likely that this codon encodes selenocysteine from the molecular weight

of the translation product and the sequence comparison data with the *Caenorhabditis elegans* homologue. The ORF codes for a protein consisting of 195 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 58 kDa. In this case, the addition of a microsomal fraction led to the formation of a product of 56 kDa from which the secretory signal is considered to have been cleaved. Since both of these products are larger than the molecular weight of 22 kDa predicted from the ORF, it is likely that the protein interacts with another protein.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein C35C5.3 (EMBL Accession No. Z78417). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein C35C5.3 (CE). U at position 49 in the amino acid sequence of the protein of the present invention represents selenocysteine. Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.9% in the entire region other than the N-terminal region. Cysteine was found in the sequence of the *C. elegans* protein at the position corresponding to position 49 encoded by the stop codon (selenocysteine) of the protein of the present invention.

Table 22

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HP MRLLLL

5 CE MRIHDELQKQDMSRFGVFIIGVLFFMSVCDVLRTEESHSHDENHVHEKDDFEAEFGDETDS  
 HP LLVAASAMVRSEASANLGGVPSKRLKMQYATGPLLKQICVSUGYRRVFEEYMRVISQRY  
 \* \*.. \*\*\* \*\*..... \* \*..

CE QSFSQGTEEDHIEVREQSSFVKPTAVHHAKDLPTLRIFYCVSCGYKQAFDQFTTFAKEY  
 HP PDIRIEGENYLPQPIYRHIAFSLSVFKLVLIIGLVGKDPFAFFGMQAPSIWQWGQENKV  
 10 \*.....\* \* ..\* \*\* \*.... \*.. \*... \*\* \* \* \* ..\*\*.

CE PNMPIEGANFAPVLWKAYVAQALSFKMAVLVLVLGGINPFERFGLGYPQILQHAHGNKM  
 HP YACMMVFFLSNMIENQCMSTGAFEITLNDVPVWSKLESGHLPMSMQQLVQILDNEMKLVNH  
 .\*\*.\*.\*.\*.\*. ....\* \*.. ..\*\*.\*.\*.\*.\* \*.....

CE SSCMLVFMLGNLVEQSLISTGAFEVYLGNEQIWSKIESGRVPSPQEFMQLIDAQLAVLGK  
 15 HP MDSIPHRS

CE APVNTESFGEFQQT

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20 Furthermore, the search of the GenBank using the base  
 sequences of the present cDNA has revealed the registration  
 of sequences that shared a homology of 90% or more (for  
 example, Accession No. AA156969) in ESTs, but, since they  
 are partial sequences, it can not be judged whether or not  
 25 any of these sequences codes for the same protein as the  
 protein of the present invention.

<HP02695> (SEQ ID Nos. 94, 104, and 114)

30 Determination of the whole base sequence of the cDNA  
 insert of clone HP02695 obtained from cDNA library of human  
 stomach cancer revealed the structure consisting of a 112-bp  
 5'-untranslated region, a 1020-bp ORF, and a 160-bp 3'-

untranslating region. The ORF codes for a protein consisting  
 of 339 amino acid residues and there existed three putative  
 transmembrane domains. Figure 34 depicts the  
 hydrophobicity/hydrophilicity profile, obtained by the Kyte-  
 Doolittle method, of the present protein. In vitro  
 translation resulted in formation of a translation product  
 of 38 kDa that was almost identical with the molecular  
 weight of 38,274 kDa predicted from the ORF.  
 The search of the protein data base using the amino  
 acid sequence of the present protein revealed that the  
 protein was similar to the rat hypertension-induced protein  
 S-2 fragment (PIR Accession No. 539959). Table 23 shows the  
 comparison between amino acid sequences of the human protein  
 of the present invention (HP) and the rat hypertension-  
 induced protein S-2 fragment (RN). Therein, the marks of -,  
 \*, and . represent a gap, an amino acid residue identical  
 with that of the protein of the present invention, and an  
 amino acid residue similar to that of the protein of the  
 present invention, respectively. The both proteins shared a  
 homology of 74.3% in the entire region.



Table 23

---

HP MNWELLWLLVLCALLLLLVQLLRFLRADGDLTLLWAEWQGRRPEWELTDMVVWVTGASS

5 HP GIGEELAYQLSKLGVSLVLSARRVHELERVKRRCLENGNLKEKDILVLPDLTDTGSHEA  
 \*\*\*\*.\*\*\*\*\*.\*\*\*.\*\*\*.  
 RN VKRRSLENGNLKEKDILVLPDLADTSSHDI  
 HP ATKAVLQEFGRIDILVNNGGMSQRSCLMDTSLDVYRKLIELNYLGTVSLTKCVLPHMIER  
 \*\*\*.\*\*\*\*\*... \*\* .\*.\*\*\*.\*\*\*.\*\*\*\*\*.\*\*\*.\*\*\*  
 10 RN ATKTVLQEFGRIDILVNNGGVAHASLVENTNMDIFKVLIEVNYLGTVSLTKCFLPHMMER  
 HP KQGKIVTVNSILGIISVPLSIGYCASKHALRGFFNGLRTELATYPGIIVSNICPGPVQSN  
 .\*\*\*\*\*...\*  
 RN NQGKIVVMKS

---

15

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T84331) in ESTs, but, since they are

20 partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10031> (SEQ ID Nos. 95, 105, and 115)

25

Determination of the whole base sequence of the cDNA insert of clone HP10031 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1464-bp ORF, and a 649-bp 3'-untranslated region. The ORF codes for a

30 protein consisting of 487 amino acid residues and there existed eleven putative transmembrane domains. Figure 35 depicts the hydrophobicity/hydrophilicity profile, obtained

by the Kyte-Doolittle method, of the present protein. In  
 vitro translation resulted in formation of a translation  
 product of high molecular weight. When expressed in COS7  
 cells, an expression product of about 55 kDa was observed in  
 the membrane fraction. 5

The search of the protein data base using the amino  
 acid sequence of the present protein revealed that the  
 protein was similar to the *Caenorhabditis elegans*  
 hypothetical protein CELK07H8 (GenBank Accession No.  
 AF047659). Table 24 shows the comparison between amino acid  
 sequences of the human protein of the present invention (HP)  
 and the *C. elegans* hypothetical protein CELK07H8 (CE).  
 Therein, the marks of -, \*, and . represent a gap, an amino  
 acid residue identical with that of the protein of the  
 present invention, and an amino acid residue similar to that  
 of the protein of the present invention, respectively. The  
 both proteins shared a homology of 44.2% in the entire  
 region. 10 15

Table 24

HP	MDGTETRQRRLDSCGKPGELGLPHPLSTGGLPVAS
5	CE MKGGGGIGDGKKDYQSAVHEGLTTFDQLGIALEDVGKSMDAETATPGGSLFSRVIFRFRN HP EDGALRAPESQSVTPKPLETEPSRETAWSIGLQVTPPFMFAGLGLSWAGMLLDYFQHWPV *...*... . . . . . *... . ** ** ***** .**... **
10	CE ENSSLKSRTYDHSNDLVNMSVIPAESSYVLFQVLPFAVAGLGMVFAGLVLSIVVTWPL HP FVEVKDLLTLVPPLVGLKGNLEMTLASRLSTAANTGQIDDPQEQHRVISSNLALIQQVAT * *. ...*...*...***** ** *...*... . * .*****.***** CE FEEIPEILILVPALLGLKGNLEMTLASRLSTLANLGHMDSSKQRKDVVIANLALVQVQAT HP VVGLLAAVAALLLGVSREEVDVAKVELLCASSVLTAFLAAFALGVLMLVCIVIGARKLG ***** * * . . . . . * * . .*****. ** *...*...*... ..
15	CE VVAFLASAFAAALAFIPSGDFDWAHGALMCASSLATAACSASLVLSLLMVVIVTSRKYNI HP NPDNIATPIAASLGLDITLSILALVSSFFFYR-HKDSRYLTPLVCLSFALTPVWVLIKQ *****.*****.*****. * * . *...*... . * . * * * * * . * . CE NPDNVATPIAASLGLDITLTVLAFFGSVFLKAHNTESWLVNIVIVLFLLLLFWIKIANE HP SPPIVKILKFGWFPIILAMVISSFGGLILSKTVSKQYKGMIFTPVICGVGGNLVAIQT . . . * ** *...*...*...***** *...*...*... . *...*...*... .*****.*..
20	CE NEGTOETLYNGWTPVIMSMISSAGGFILETAV--RRYHSLSTYGPVLNGVGGNLAAVQA HP SRISTYLHMWSAPGVLPLQ--MKKFWPNPCSTFCTSEINSMARSARVLLLLLVPGHLIF-FY **.*...*... . . ***** . . . * . . . * . * .*****. * * CE SRLSTYFHKAGTVGVLPNEWTVSRF--TSVQRAFFSKEWDSRSARVLLLLLVPGHICNFL HP I-IYLVEGQSVINSQ--TFVVLYLLAGLIQVTILLYLAEVMVRLTWHQALDPDNHCIPYL
25	* .. . . . . . * .*****.*****. . . * * * . ***** **** CE IQLFTLTSKNNVTPHGPLFTSLYMIAAIIQVVILLFVCQLLVALLWKWKIDPDNSVIPYL HP TGLGDLGTLGLLALCFFTDWLLKSKAELGGISELASGPP * .*****. * . * CE TALGDLLGTGLLFIVFLTTDHFDPKELTSS
30	

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA334000) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5

<HP10530> (SEQ ID Nos. 96, 106, and 116)

Determination of the whole base sequence of the cDNA insert of clone HP10530 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 80-bp 5'-untranslated region, a 1182-bp ORF, and a 95-bp 3'-untranslated region. The ORF codes for a protein consisting of 393 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 36 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 46 kDa that was somewhat larger than the molecular weight of 44,912 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 45.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 23. When expressed in COS7 cells, an expression product of about 43 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein IG002N01 (Genbank Accession No. AF007269). Table 25 shows the comparison between amino acid sequences of the

human protein of the present invention (HP) and the A. thaliana hypothetical protein IG002N01 (AT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 27.0% in the N-terminal region of 355 amino acid residues.

Table 25

HP  
MRTLFNLTWL

5 AT MELTSFQKSPSSNDVVSFSVSLVRNSMARRRSSAAESLKRNDGYESTLCQVVQDSDRR

HP ALACSPVHTTLLSKSDAKKAAASKTLLKESQFSQDQVQDRGLVTDLKAESVLEHRSYCSA

.....

AT LITFIVIFIVIPAVISAIVYKVKFADRVIQTESIRQKGIKTDINFGIITESHK--AS

HP KARDRHFAGDVLGVTPWNSHGVDVTKVFGSKFTQISPVWLQ-LKRRGRREMEFEVTLHDV

10 ..... \* \* \* \* \*

AT ENSTRHYDYPVLAYITP--CQSGSL--VLEGR-HNADKGMWIOELRSRGNATSAKGLPKL

HP DQGMRAVAKKHAAGLHIVPRLTFEDWTYDDFRNVLDSEDEIEELSKTIVVQVAKNQHFDF

..... \* \* \* \* \*

AT ---YNSCIFHATKRMNFFTLIELVNFNNTYLVIMFALNS-REMEYNGIIVLESWSRMAAYGLV

15 HP VEVWNQLLSQKRVGLIHMLTHLAELHQARLATLVIPPAITPGTDQLGMFTKHKEFQI

..... \* \* \* \* \*

AT HDPDLKMATKFKVQKGLGDALHSTSPRNQOHMQFMVVGPPRSEKLMQYDFEPDLQFI

HP APVLDFSLMTYDYSTAHOEPGNAPLSWVRACVQ-VLDPKSK---WRSKILGLNFGM

..... \* \* \* \* \*

20 AT KDSVDGFSMTYDFSNPQNPBPNAFVKWIDLTLLGSSNNIDSNIAKRVLLGINFYGN

HP DYATSKDAREPVPVGAHYIQTLLKDHRRPMWVSDQASFEHFFIYKKSRSRSGRHVVFFPTLKSLQ

..... \* \* \* \* \*

AT DVAISGGGGAITGRDYIALTLQKHKKPTFRWDKESGHEHLMYVRDDKNIKKHAAYFPITMSIL

25 HP VRLTEARELGVSISWELGQGLDYFYDLL

AT LRLENARLWIGISISWIEIGQDKGHGFKKYYAASALBASISFSGHTFDMQFRITNPRQLSRNGS

30 Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA302913) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the

protein of the present invention.

<HP10541> (SEQ ID Nos. 97, 107, and 117)

Determination of the whole base sequence of the cDNA  
5 insert of clone HP10541 obtained from cDNA library of human  
stomach cancer revealed the structure consisting of a 7-bp  
5'-untranslated region, a 591-bp ORF, and a 113-bp 3'-  
untranslated region. The ORF codes for a protein consisting  
of 196 amino acid residues and there existed a putative  
10 secretory signal at the N-terminus. Figure 37 depicts the  
hydrophobicity/hydrophilicity profile, obtained by the Kyte-  
Doolittle method, of the present protein. In vitro  
translation resulted in formation of a translation product  
of 23 kDa that was somewhat larger than the molecular weight  
15 of 21,553 predicted from the ORF. In this case, the addition  
of a microsome led to the formation of a product of 20 kDa  
from which the secretory signal is considered to have been  
cleaved and a product of 23 kDa which is considered to have  
a sugar chain being attached. Application of the (-3,-1)  
20 rule, a method for predicting the cleavage site of the  
secretory signal sequence, allows to expect that the mature  
protein starts from glycine at position 41. In addition,  
there exists in the amino acid sequence of this protein one  
site at which N-glycosylation may occur (Asn-Leu-Thr at  
25 position 185).

The search of the protein data base using the amino  
acid sequence of the present protein revealed that the  
protein was similar to the human zymogen membrane protein  
(GenBank Accession No. AF056492). Table 26 shows the  
30 comparison between amino acid sequences of the human protein  
of the present invention (HP) and the human zymogen membrane  
protein (ZM). Therein, the marks of -, \*, and . represent a

10	HP MWRVPGTTRRPVLTGESPGMHRPFEAMLLLLLTLALGGLTWAGKMYGCGGCKYFS-TTEDDY	
	MTVAATLALCASASGNALQARSSSYSGEYSGSGGKRFSSHSGNQLD	
	HP HEITGLRVSVGLLVKKSQVQKLGDSWDVKLGALGNTOEVTLPGEZYITKVFAFAQLR	
	*****	
	*****	
	ZM GPITALRVRVNTYYIVGLQVRKYGKWSVDYVGGRNGDLEIFLHPGESVIVQSGKYYKWLK	
15	HP GWMYNTSKDRYFFYFGKLDGQISSAYPSQEGVLVGIYGYQLGIKISIGFEWN-YPLEP	
	*****	
	ZM KLFVETDKGRYLSFGKDSGTGFNAVPLHPNTVLRFISGRSGSL-IDAIGLHWDVYPTSCS	
	HP TTEPPVNILTYSANSPVGR	
20	ZM RC	
25	<p>Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA340605) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.</p>	

25 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA340605) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.



insert of clone HP10550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 241-bp 5'-untranslated region, a 324-bp ORF, and a 86-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 38 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA348310) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10590> (SEQ ID Nos. 99, 109, and 119)

Determination of the whole base sequence of the cDNA insert of clone HP10590 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 77-bp 5'-untranslated region, a 1053-bp ORF, and a 180-bp 3'-untranslated region. The ORF codes for a protein consisting of 350 amino acid residues and there existed one putative transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,285 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of

43 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Ser at position 144 and Asn-Leu-Thr at position 328).

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA461346) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10591> (SEQ ID Nos. 100, 110, and 120)

Determination of the whole base sequence of the cDNA insert of clone HP10591 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 232-bp 5'-untranslated region, a 324-bp ORF, and a 844-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,328 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H09424) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

of the present invention.

<HP01462> (SEQ ID Nos. 121, 131, and 141)

5 Determination of the whole base sequence of the cDNA  
insert of clone HP01462 obtained from cDNA library of human  
fibrosarcoma cell line HT-1080 revealed the structure  
consisting of a 121-bp 5'-untranslated region, a 1452-bp ORF,  
and a 477-bp 3'-untranslated region. The ORF codes for a  
protein consisting of 483 amino acid residues and there  
10 existed a putative secretory signal at the N-terminus.  
Figure 41 depicts the hydrophobicity/hydrophilicity profile,  
obtained by the Kyte-Doolittle method, of the present  
protein. In vitro translation resulted in formation of a  
translation product of 72 kDa that was larger than the  
15 molecular weight of 55,838 predicted from the ORF.  
Application of the (-3,-1) rule, a method for predicting the  
cleavage site of the secretory signal sequence, allows to  
expect that the mature protein starts from lysine at  
position 21.

20 The search of the protein data base using the amino  
acid sequence of the present protein revealed that the  
protein was similar to the *Caenorhabditis elegans*  
hypothetical protein ZK1058.4 (EMBL Accession No. Z35604).  
Table 27 shows the comparison between amino acid sequences  
25 of the human protein of the present invention (HP) and the *C.*  
*elegans* hypothetical protein ZK1058.4 (CE). Therein, the  
marks of -, \*, and . represent a gap, an amino acid residue  
identical with that of the protein of the present invention,  
and an amino acid residue similar to that of the protein of  
30 the present invention, respectively. The both proteins  
shared a homology of 35.6% in the entire region.

Table 27

	HP MKAFHHTFCVLLTVFGSSVSAKFDDEDEEDIVEYDNDNDAFFEDVMEBSVTESPQRIIT	
	CE MKIWMIFLIFIGFAIST	5
	HP EDDE-DETTVELEGGDENGGDEGDEADTQEGDTESEPPYDDERFEGYDKP-----D	
	CE DNEFAFEFEDEFEVSSATQAPBEIQREGEPPVLKQKDDFEEDDFGVVEEPEEAEKVREAD	
	HP TSSSKNKDPITIVDPAHLQNSWESYYLEILMTGLTAYIMNYIIIGKNKNSRLAQAWNT	10
	CE SDDAAPAQPALKFADVPARFRSNWASYQVEGIVVLIILIMTNYLIGKTTNASIAQTIDM	
	HP HRELTESNFTLVGDGNTNKEATSTGKLNQENEHIIYNTLWCSGRVCCGMLIQLRFLKRQDL	
	CE CRPTLEEQFAVGDGTTDLDKMIPISTKHDTSTSSAWCTGRVNVNSLFLQMKMVKRQDV	15
	HP INVLAARMRPVSDQVQIKVTMN-DEMDTYYVFAVGTRKATVRLQKEMQDLSFECSDKPKS	
	CE VSRIMEMFTSPSGDKMTIKASLETTNDTDLIFAVGEKKIASKYFKEMLDLNSFASERKQA	
	HP GAKYGLPDSLALISEMGEVTDGMDTKMVHFLTHYADKIESVHFSDQFSGPKIMQEEGQP	
20	CE AQQFNLPASWQVYADQNEVVFSLDPPGVSLTKKHEDAEIHFIIHISDQFTGPKPAEGESYT	
	HP LKLPDTKRITLFTFNVPFSGNTYPPKDMEALPLIMNMVYISIDKAKKFRILNRREGKQKADKN	
	CE -RLPEAQRYMVFVSLNLQVILG----QDEESVMEIITLVLYLIDKAKKMKLSKDAKVKAEER	
	HP RARVEENFLKLTHTVQREAAQSRREKKRAEKEKERIMNEEDPEKQRLTEAALRRERQKLE	25
	CE RKEFEADFLKQTHQFRQEAQARREKTKRERKQKTLMDSPFERQRLTEAKELKRRAKA--	
	HP KKQMKKQIKVKAM	
	CE -KSPKMKQILKVK	30

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA307793) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5

<HP02485> (SEQ ID Nos. 122, 132, and 142)

Determination of the whole base sequence of the cDNA insert of clone HP02485 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 69-bp  
10 5'-untranslated region, a 1005-bp ORF, and a 1672-bp 3'-untranslated region. The ORF codes for a protein consisting of 334 amino acid residues and there existed one putative transmembrane domain. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-  
15 Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 38,171 predicted from the ORF. When expressed in COS7 cells, an expression product of about 23 kDa was  
20 observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein W01A11.2 (GenBank Accession No. U64852).  
25 Table 28 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein W01A11.2 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of  
30 the present invention, respectively. The both proteins shared a homology of 45.5% in the entire region.

Table 28

HP MVEFAPLFMPWERRLQTLAVLQFVFSFIALAEICT-V  
\*\*\*\*\*

CE MRLTSSISGAKLPDKKICSSVSRIAPLPLVPWKRRLETLAVMGFIEMWVILPIMDLWV  
HP GFIALTLTRFWLLTVLYAAWVYLDKDKPRQGGKHIGAIRCWTIWKYMKDYFPISTLVKTAE  
\*\*\*\*\*

CE PFHVLNTRWVTLVPLYYAVWFYDDFTPKKASRRRWVARRHVAWKYFASYPPLRIKLTAD  
HP LDPSSNYIAGFHPHGVLAVGAFANLCTESTGESSIFPGIRPHLMMLTLWFRAPFFRDYIM  
\*\*\*\*\*

CE LPADRNYIIGSHPHGMFSVGGFTAMSTNATGFEEDKFFPGIKSHIMTLNNGQFFPFRREFGI  
HP SAGLVTSKESAAHILNRKGGGNLTGIIIVGAQEAALDARPGSFLLILNRKGGFVRALATH  
\*\*\*\*\*

CE MLGIEVSKESLEYTLTKCGKGRACAIVIGASAEALTAHPNKNNTLLINRGGFCCKYALKF  
HP GATLVIFSGENDLFDQIPNSSGSWLRKIYIQRNLQKIMGISLPLFHGRGVF-QYSFGLIP  
\*\*\*\*\*

CE GADLVPMYNGENDLYRQYENPNKGSRLREVQEKIKDMFGLCPPLLRGRSLFNQYLLIGLIP  
HP YRRLITTVVGKPIEVQKTLHPSEEEVNQHLHQRYIKELCNLFEAHKLKLFNIPADQHLHFC  
\*\*\*\*\*

CE FRKPVITVWGRPIRVTQTDEPPTWEQIDELHAKYCDALYNLFEEYKHLHSIPDPDTHLIFQ  
\*\*\*\*\*

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D25664) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02798> (SEQ ID Nos. 123, 133, and 143)

Determination of the whole base sequence of the cDNA

insert of clone HP02798 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 31-bp 5'-untranslated region, a 804-bp ORF, and a 301-bp 3'-untranslated region. The ORF codes for a protein consisting of 267 amino acid residues and there existed four putative transmembrane domains. Figure 43 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 30,778 predicted from the ORF. When expressed in COS7 cells, an expression product of about 26 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human DHHC-containing cysteine-rich protein (GenBank Accession No. U90653). Table 29 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human DHHC-containing cysteine-rich protein (DH). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.0% in the intermediate region of 100 amino acid residues. The positions of seven cysteines were conserved between the two proteins. The protein of the present invention also had the DHHC (Asp-His-His-Cys) sequence.

Table 29

HP MAPWALLSPGVLRITGHTVLTWGI

5 DH MYKMNICNKPNSNKTAPKSVWTAPAPSPSPETLGGQSRKRNQSWSPHPHILQIVAWLLYL

HP TLVTLFHDTELRQWEEQGEILLPLTFLTLVLSLTLVLAWSLMDPGYVNVQPP-QEELK

\* \* \* \* \*

DH FFAVIGFGLVPLPHHWPVPAAGYACMGALFAGHLVHTLAVSIDPADNVDRDKSYAGPLP

HP EQOTAMVPPAIPLRRCRYCGLVLPRLARHRCRCRQVRRYDHHCHCPMMENCGEERNHPLFV

10 HP \*\*\*\*\* \* \* \* \* \*

DH IFNRQHAHVIEDLHCNLCNVDSARSKKHCACNKCVCGCFDHHCKWLNNGVGEERNYRLFL

HP VYIALQVLVLTWGLYLAWSGLRFFQPWGLWRSSGLLFAITFLTLTSLFSLVASTLTVSHLY

\* \* \* \* \*

DH HVSASATLGVLLTLVLTGGHICLRGVLCQPHASAHQFTL

15  
20 Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D79050) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10041> (SEQ ID Nos. 124, 134, and 144)  
determination of the whole base sequence of the cDNA insert of clone HP10041 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 12-bp 5'-untranslated region, a 321-bp ORF, and a 286-bp 3'-untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 44 depicts



the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 12,060 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein K10B2.4 (GenBank Accession No. U28730). Table 30 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein K10B2.4 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 62.1% in the entire region.

Table 30

---

	HP	MSTNNMSDPRRPKNKVLRYKP---PPSECNPALDDPTPDYMNLLGMIFSMCGLMLKLKWC
		.****.*.....** *.....*****.....
25	CE	MQQNGDPRRTNRIVRYKPLDSTANQQQAISEDPLPEYMNVLGMIFSMCGLMIRMKWCS
	HP	WVAVYCSFISFANSRSEDTKQMMSSFMLSISAVVMSYLQNPQPMTPPW
		*.* ** *****.*.*.*.....*****.***** *..***
	CE	WLALVCSCISFANTRTSDDAKQIVSSFMLSVSAVVMSYLQNPSPPIPPWVTLQ

---

Furthermore, the search of the GenBank using the base

5 sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H20098) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10246> (SEQ ID Nos. 125, 135, and 145)

10 Determination of the whole base sequence of the cDNA insert of clone HP10246 obtained from cDNA library of human epidermoid carcinoma cell line KB revealed the structure consisting of a 110-bp 5'-untranslated region, a 675-bp ORF, and a 79-bp 3'-untranslated region. The ORF codes for a protein consisting of 224 amino acid residues and there existed five putative transmembrane domains. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat smaller than the molecular weight of 25,244 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the membrane fraction.

25 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human putative seven transmembrane domain protein (GenBank Accession No. Y18007). Table 31 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human putative seven transmembrane domain protein (TM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

of the protein of the present invention, respectively. The both proteins shared a homology of 93.3% in the entire region.

5

Table 31

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HP MTLFHFNGCFALAYFPYFITYKCSGLSEYNAFWKCVQAGVTYLFVQLCKMLFLATFFPTW
*****.*****
TM MTLFHFNGCFALAYFPYFITYKCTDLSEYNAFWKCVQAGVTYLFVQLCKMLFLATFFPTW
10 HP EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
*****
TM EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
HP VGARGIEFDWKYIQMSIDSNISLVHYIVASAQVWMITRYDLYHTFRPAVLLLMFLSVYKA
*****.*****
15 TM VGARGIEFDWKYIQMSIDSNISLGPYIVASAQVWMITRYDLYHTFRPAVLLLMFLRVYKA
HP FVMETFVHLCSLGSLGWAALLARAVVTGLLALSTLALYVAVVNVHS
*****.***.***.***.***.***.***
TM FVMETFVHLCSLGSLGWAFLMAGVVVKGLLVIRNLAMYVAVVNVHS

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20

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA453931) in ESTs, but, since they

25 are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10392> (SEQ ID Nos. 126, 136, and 146)

30

Determination of the whole base sequence of the cDNA insert of clone HP10392 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure

consisting of a 24-bp 5'-untranslated region, a 777-bp ORF, and a 726-bp 3'-untranslated region. The ORF codes for a protein consisting of 258 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was somewhat larger than the molecular weight of 29,623 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 49.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H15999) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention. In addition, partial identity with the hypothetical protein KIAA0384 (Accession No. AB002382) was observed, although the hypothetical protein had a different ORF.

<HP10489> (SEQ ID Nos. 127, 137, and 147)

Determination of the whole base sequence of the cDNA insert of clone HP10489 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 137-bp 5'-untranslated region, a 333-bp ORF, and a 189-bp 3'-untranslated region. The ORF codes for a protein consisting of 110 amino acid residues and there existed two putative transmembrane domains. Figure 47 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 12,010 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA262162) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10519> (SEQ ID Nos. 128, 138, and 148)

Determination of the whole base sequence of the cDNA insert of clone HP10519 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 67-bp 5'-untranslated region, a 276-bp ORF, and a 367-bp 3'-untranslated region. The ORF codes for a protein consisting of 91 amino acid residues and there existed one putative transmembrane domain. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,275 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W16639) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

of the present invention.

<HP10531> (SEQ ID Nos. 129, 139, and 149)

Determination of the whole base sequence of the cDNA

5 insert of clone HP10531 obtained from cDNA library of human

osteosarcoma cell line Saos-2 revealed the structure

consisting of a 55-bp 5'-untranslated region, a 1035-bp ORF,

and a 1092-bp 3'-untranslated region. The ORF codes for a

protein consisting of 344 amino acid residues and there

10 existed five putative transmembrane domains. Figure 49

depicts the hydrophobicity/hydrophilicity profile, obtained

by the Kyte-Doolittle method, of the present protein. In

vitro translation resulted in formation of a translation

product of high molecular weight.

15 Furthermore, the search of the GenBank using the base

sequences of the present cDNA has revealed the registration

of sequences that shared a homology of 90% or more (for

example, Accession No. R50695) in ESTs, but, since they are

20 partial sequences, it can not be judged whether or not any

of these sequences codes for the same protein as the protein

of the present invention.

<HP10574> (SEQ ID Nos. 130, 140, and 150)

Determination of the whole base sequence of the cDNA

25 insert of clone HP10574 obtained from cDNA library of human

stomach cancer revealed the structure consisting of a 210-bp

5'-untranslated region, a 1287-bp ORF, and a 1276-bp 3'-

untranslated region. The ORF codes for a protein consisting

30 of 428 amino acid residues and there existed a putative

secretory signal at the N-terminus and one putative

transmembrane domain in the intermediate region. Figure 50

depicts the hydrophobicity/hydrophilicity profile, obtained

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 36.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Drosophila melanogaster* GOLIATH protein (SWISS-PROT Accession No. Q06003). Table 32 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *D. melanogaster* GOLIATH protein (DM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The intermediate region of 169 amino acids of the protein of the present invention shared a homology of 41.4% with the N-terminal region of the *D. melanogaster* GOLIATH protein.

Table 32

HP MGPPGAGVSCRGCGGFSRLTAWCFLTALSPQAPGSRGAEAVWTAYLNVSWRVPHHTGVNR  
HP TVWELSEEGVYGQDSPLEPVAAGVLVPDPGALNACNPHNTNFTVPTWGSTVQVSWLALI  
HP QRGCGCTFADKIHLYERGAAGAVIFNFPBGTRNEVIFPMSHPGADVAIMIGNLKGTKIL

DM  
MQLKMQIKGKTRNIAAVITYQNIQDLS  
HP QSIQRGIQVTMIVBVGKK---HGPWVNNHYSIFFVSFFIITATVGYFIFYSARRLRNA  
.....  
DM LTLDKGYNVLTISIIEGRGVRRTISSLNRTSVLFVIS-FIV-DDILCWLIFYYIQRFRYM

HP RAQSRKQRLKADAKKAIGRLQLRTLKQGDKEIGDPDSCAVCIBLYKPNDLVRLITCNH  
.....  
DM QAKDQSRNLCSTVTKKAIMKIPITKTKGKFS-D-EKDLDSDCCALCIEAYKPTDITRILIPCKH  
HP IEHKTCVDPWLTIEHRTCPMCKCDILKALGIEVDGDSVSLQVPVSNFISNSASSHEEDN  
\*\*\*\*\*

DM EFHKNCIDPWLTIEHRTCPMCKLDVLKFKYGVVGDQIYQTPSPQHTAPIASIEEVPVIVA  
HP RSETASSGYASVGTDPEPPLTEHHVQSTNESLQLVNHHEANSVAVDVIPIHVDNPTFEEDETP  
DM VFHGPPLQLQASNMSSFAFSHYFQSSRSPPSSSVQQLAPLTYQHPHQQAASERGRNRS  
HP NQETAVREIKS  
DM APATMPHAIITASHQVTDV

25 Furthermore, the search of the GenBank using the base  
sequences of the present cDNA has revealed the registration  
of sequences that shared a homology of 90% or more (for  
example, Accession No. A4155685) in ESTs, but, since they  
are partial sequences, it can not be judged whether or not  
any of these sequences codes for the same protein as the  
30 protein of the present invention.



The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. All of the proteins of the present invention are secreted or exist in the cell membrane, so that they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or the differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for large-scale expression of these proteins. Cells into which these genes are introduced to express these proteins, can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or

primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein).

Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished

through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s). Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more

5 preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

10 Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

25 The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide, which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

30 The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides

capable of hybridizing under reduced stringency conditions,  
more preferably stringent conditions, and most preferably  
highly stringent conditions, to polynucleotides described  
herein. Examples of stringency conditions are shown in the  
5 table 33 below: highly stringent conditions are those that  
are at least as stringent as, for example, conditions A-F;  
stringent conditions are at least as stringent as, for  
example, conditions G-L; and reduced stringency conditions  
are at least as stringent as, for example, conditions M-R.

Table 33

Stringency Condition	Polynucleotide Hybrid Length (bp) <sup>†</sup>	Hybridization Temperature and Buffer <sup>†</sup>	Wash Temperature and Buffer <sup>†</sup>
A	DNA : DNA	≥50	65°C; 1×SSC -or- 42°C; 1×SSC, 50% formamide
B	DNA : DNA	<50	T <sub>B</sub> <sup>*</sup> ; 1×SSC
C	DNA : RNA	≥50	67°C; 1×SSC -or- 45°C; 1×SSC, 50% formamide
D	DNA : RNA	<50	T <sub>D</sub> <sup>*</sup> ; 1×SSC
E	RNA : RNA	≥50	70°C; 1×SSC -or- 50°C; 1×SSC, 50% formamide
F	RNA : RNA	<50	T <sub>F</sub> <sup>*</sup> ; 1×SSC
G	DNA : DNA	≥50	65°C; 4×SSC -or- 42°C; 4×SSC, 50% formamide
H	DNA : DNA	<50	T <sub>H</sub> <sup>*</sup> ; 4×SSC
I	DNA : RNA	≥50	67°C; 4×SSC -or- 45°C; 4×SSC, 50% formamide
J	DNA : RNA	<50	T <sub>J</sub> <sup>*</sup> ; 4×SSC
K	RNA : RNA	≥50	70°C; 4×SSC -or- 50°C; 4×SSC, 50% formamide
L	RNA : RNA	<50	T <sub>L</sub> <sup>*</sup> ; 2×SSC
M	DNA : DNA	≥50	50°C; 4×SSC -or- 40°C; 6×SSC, 50% formamide
N	DNA : DNA	<50	T <sub>N</sub> <sup>*</sup> ; 6×SSC
O	DNA : RNA	≥50	55°C; 4×SSC -or- 42°C; 6×SSC, 50% formamide
P	DNA : RNA	<50	T <sub>P</sub> <sup>*</sup> ; 6×SSC
Q	RNA : RNA	≥50	60°C; 4×SSC -or- 45°C; 6×SSC, 50% formamide
R	RNA : RNA	<50	T <sub>R</sub> <sup>*</sup> ; 4×SSC

†: The hybrid length is that anticipated for the hybridized region(s) of the

hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

†: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub> and 1.25mM EDTA, pH7.4)

can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after

hybridization is complete.

\*T<sub>B</sub> - T<sub>R</sub>: The hybridization temperature for hybrids anticipated to be less than

50 base pairs in length should be 5-10°C less than the melting temperature ( $T_m$ ) of the hybrid, where  $T_m$  is determined according to the following equations. For hybrids less than 18 base pairs in length,  $T_m(^{\circ}\text{C}) = 2(\text{\# of A + T bases}) + 4(\text{\# of G + C bases})$ . For hybrids between 18 and 49 base pairs in length,  $T_m(^{\circ}\text{C}) = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\% \text{G+C}) - (600/N)$ , where N is the number of bases in the hybrid, and  $[\text{Na}^+]$  is the concentration of sodium ions in the hybridization buffer ( $[\text{Na}^+]$  for  $1\times\text{SSC}=0.165\text{M}$ ).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

1. A protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. 5

2. An isolated DNA coding for the protein according to claim 1. 10

3. An isolated cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140. 15

4. The cDNA according to claim 3 consisting of any one of a base sequence selected from the group consisting of SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. 20

5. An expression vector that is capable of expressing the DNA according to any one of claim 2 to claim 4 by in vitro translation or in eucaryotic cells. 25

6. A transformed eucaryotic cell that is capable of expressing the DNA according to any one of claim 2 to claim 4 and of producing the protein according to claim 1. 30

# CLAIMS



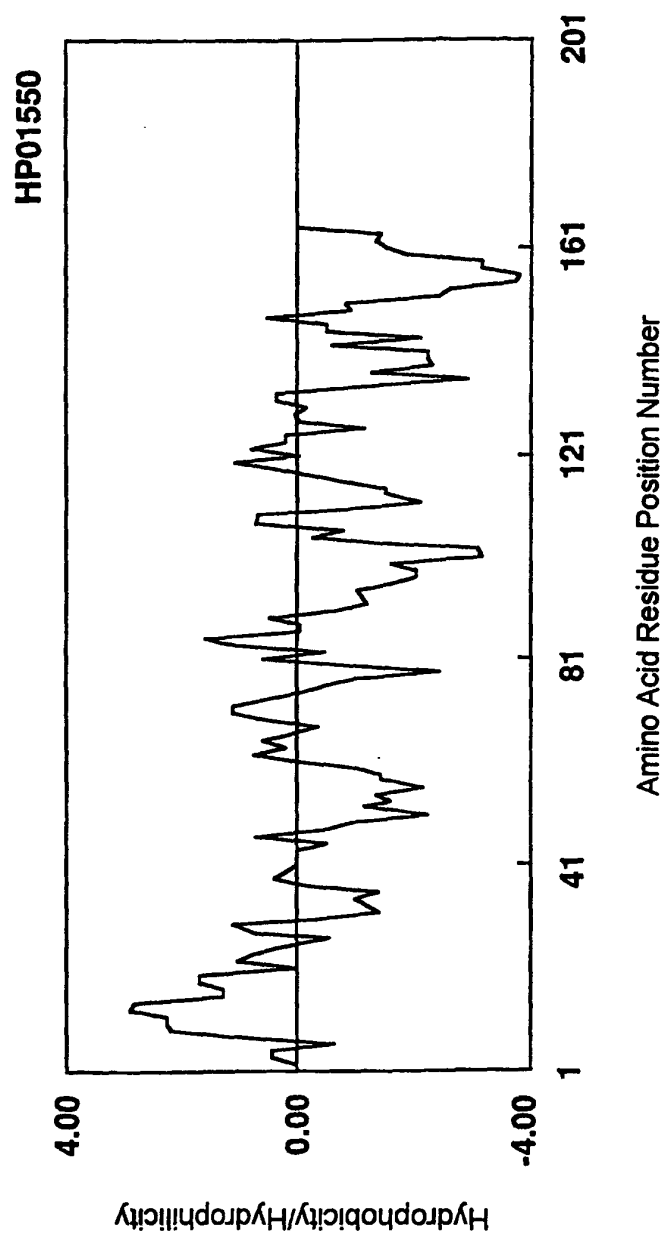


Fig. 1

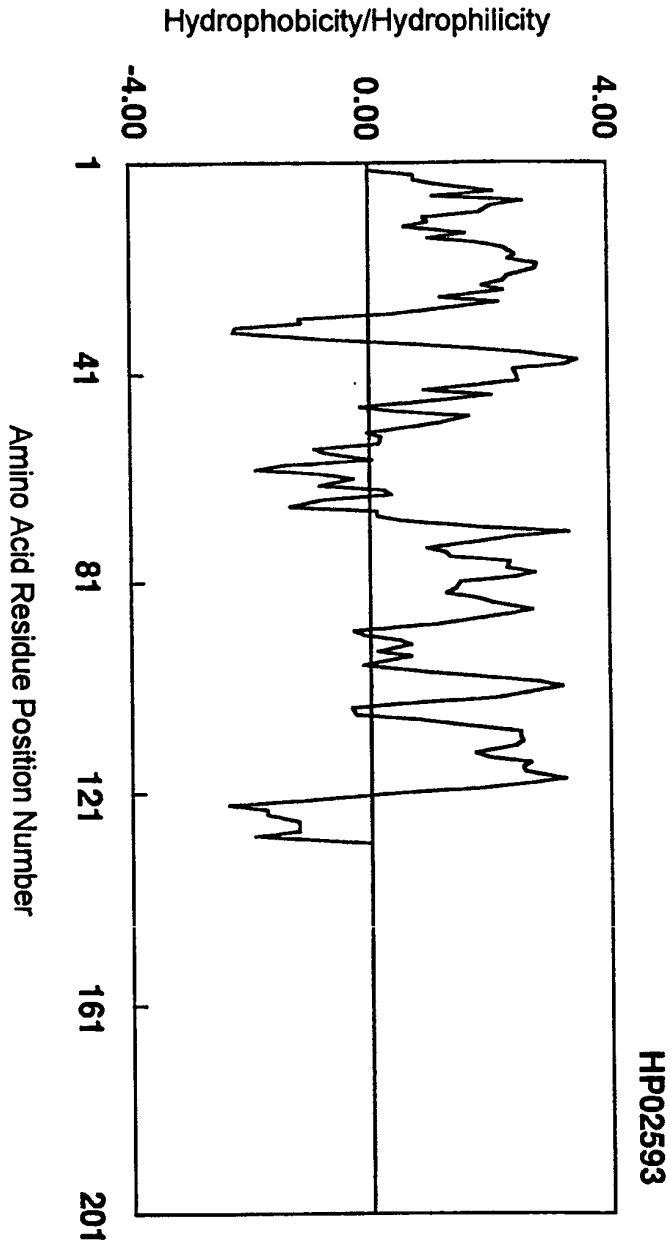


Fig. 2

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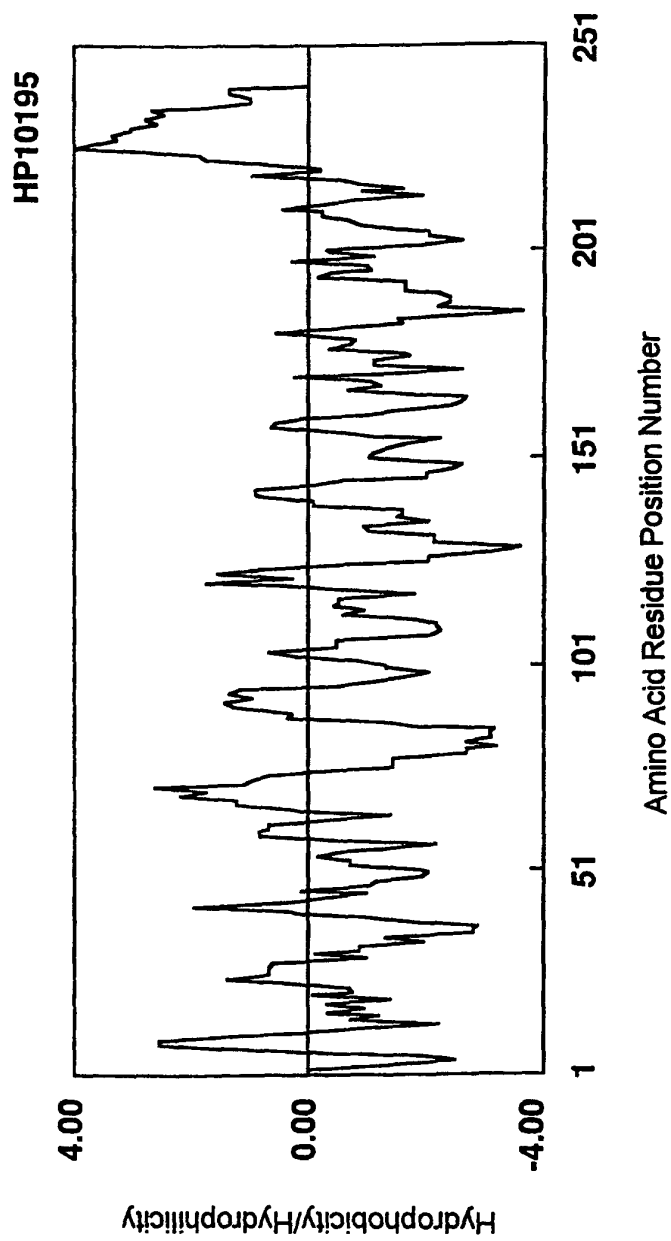


Fig. 3

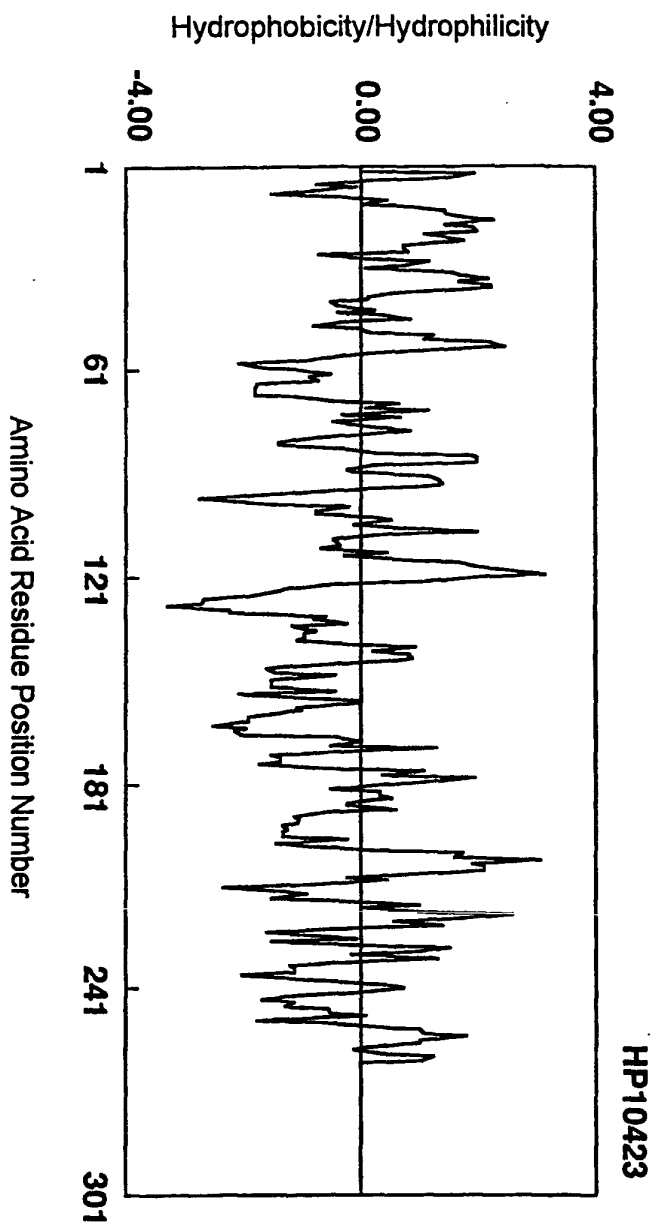


Fig. 4

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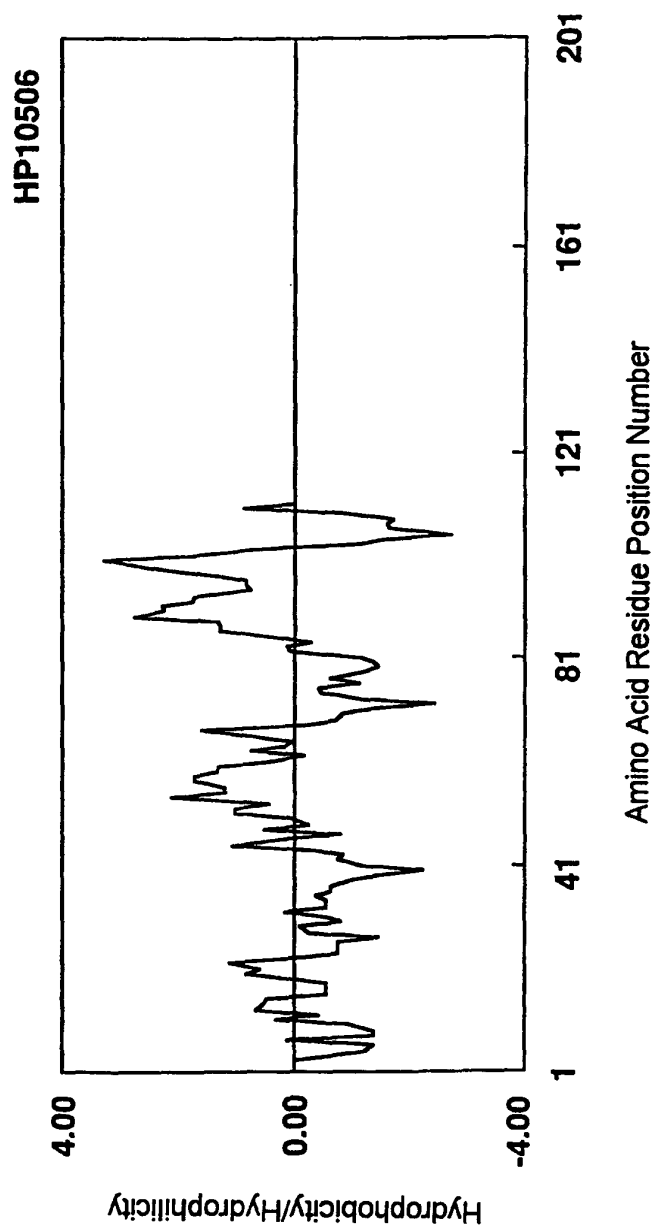


Fig. 5

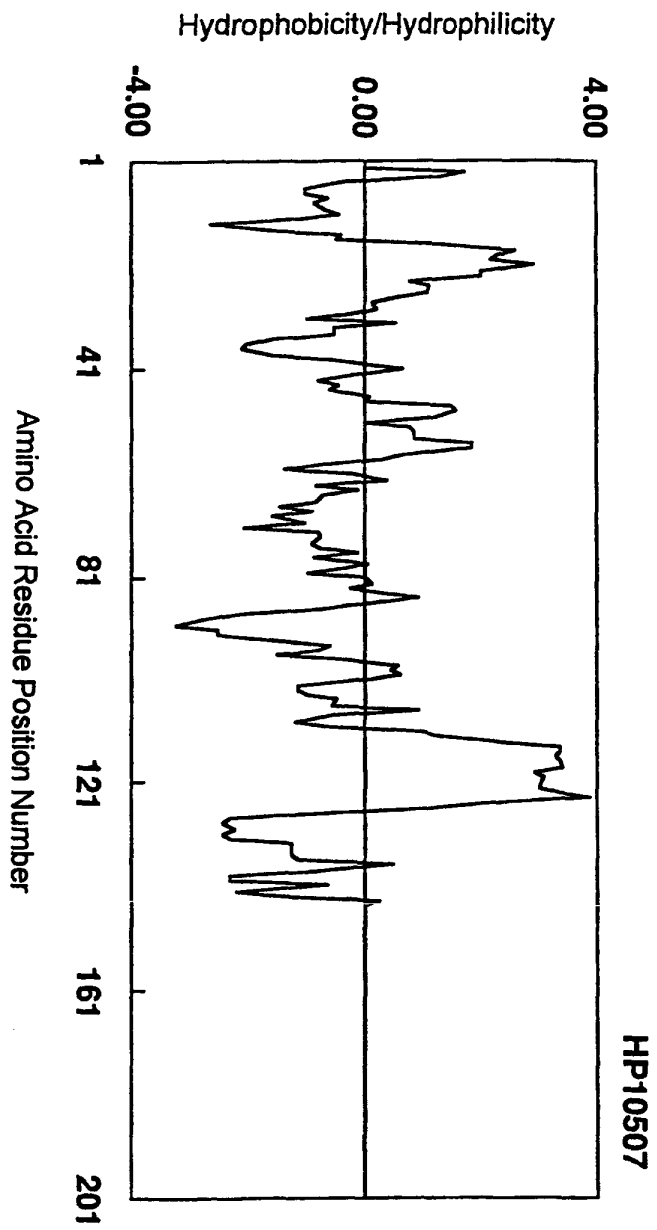


Fig. 6

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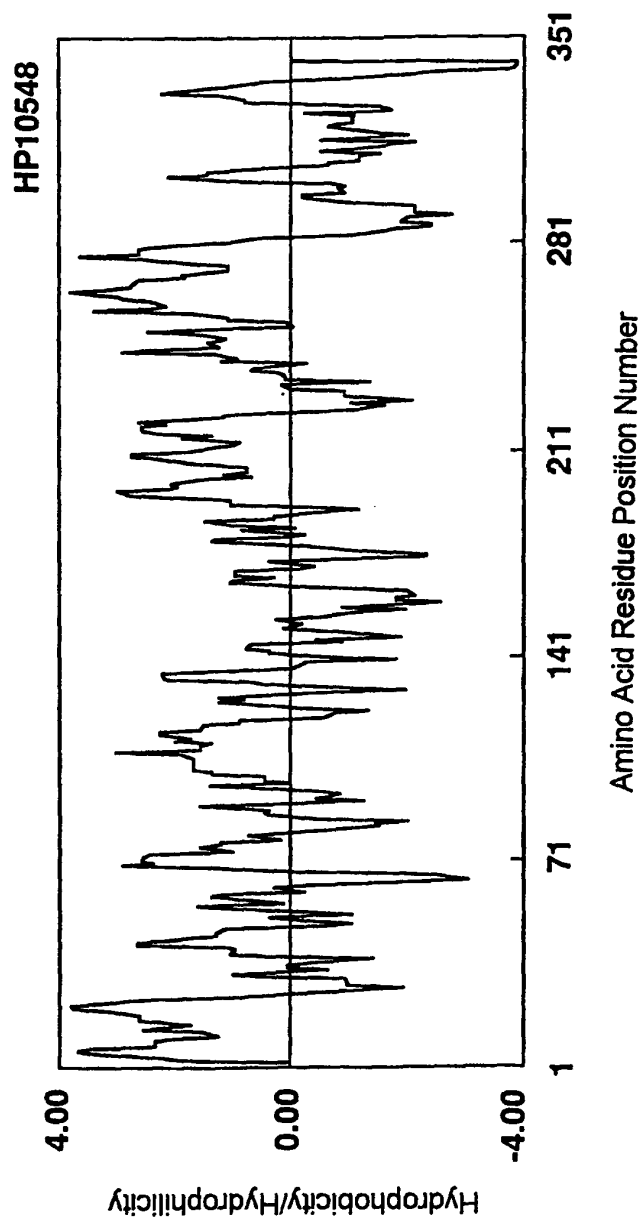


Fig. 7

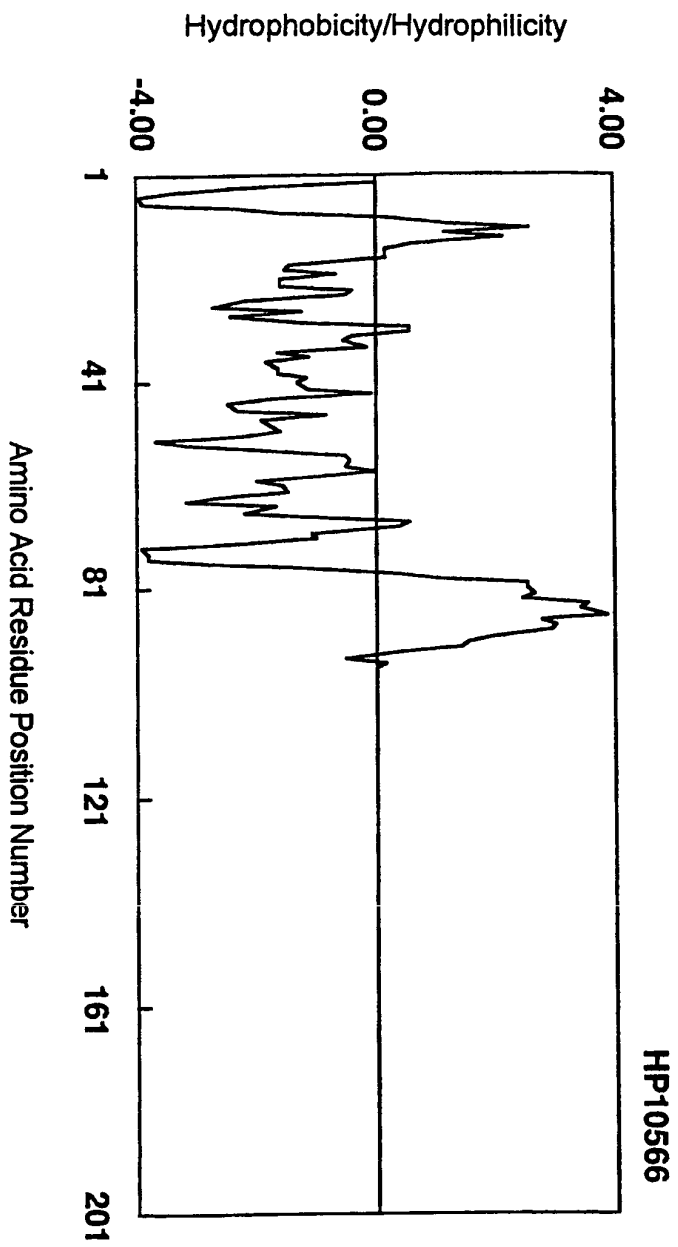


Fig. 8



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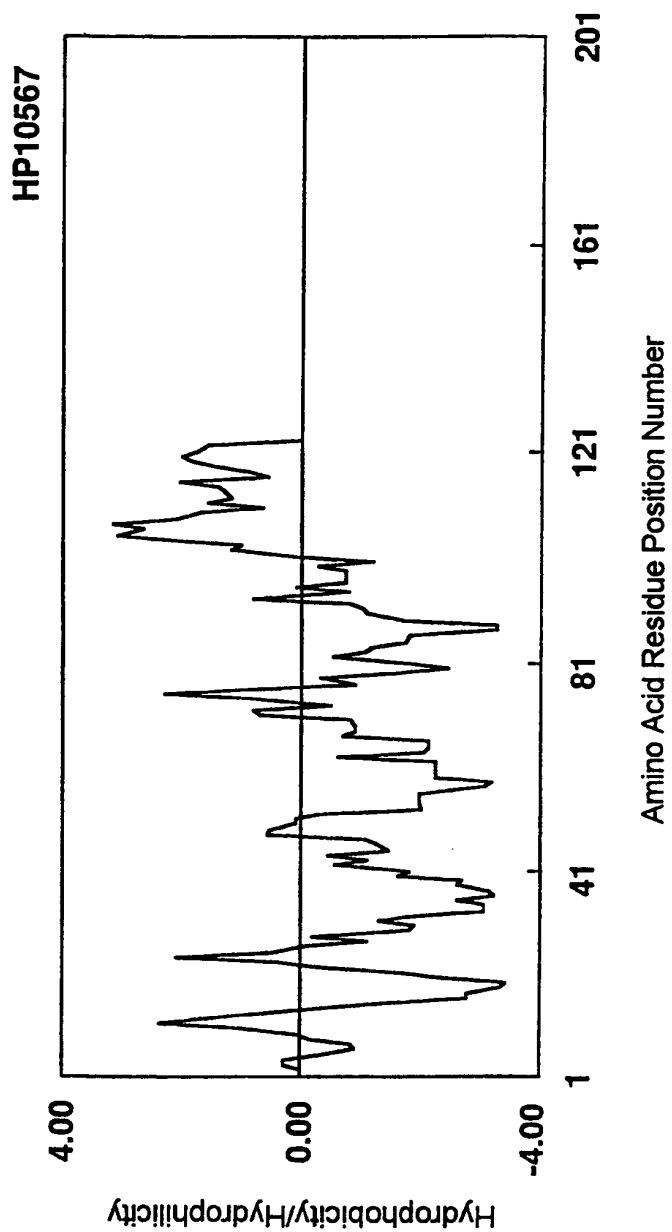


Fig. 9

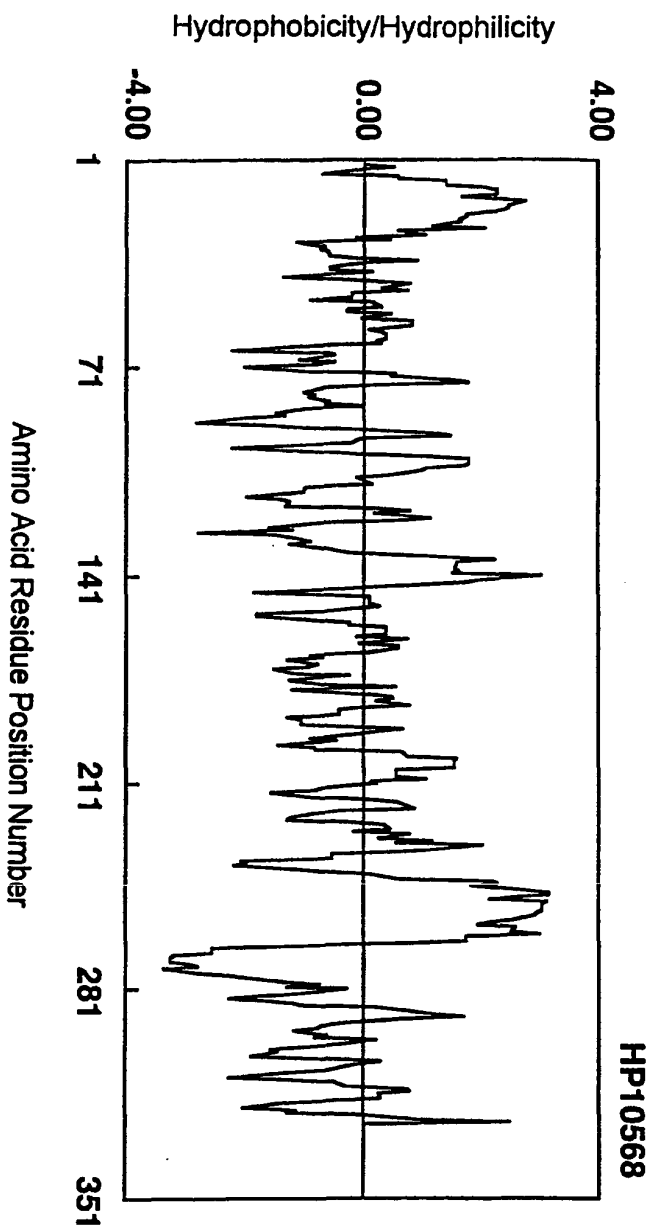


Fig. 10

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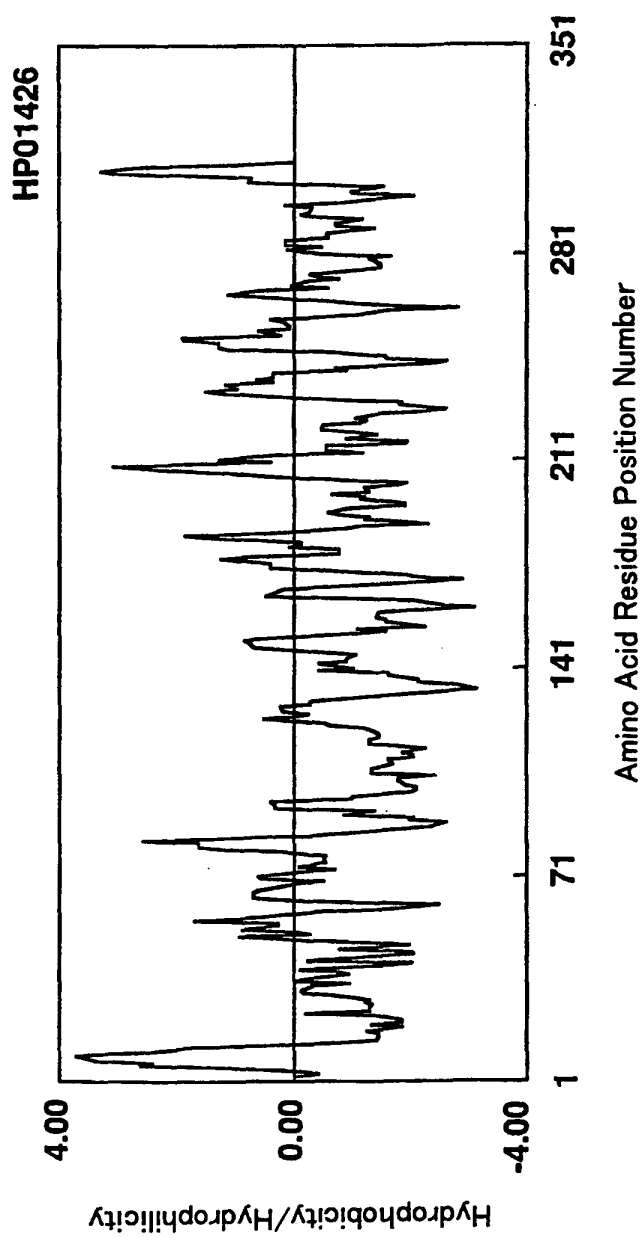


Fig. 11

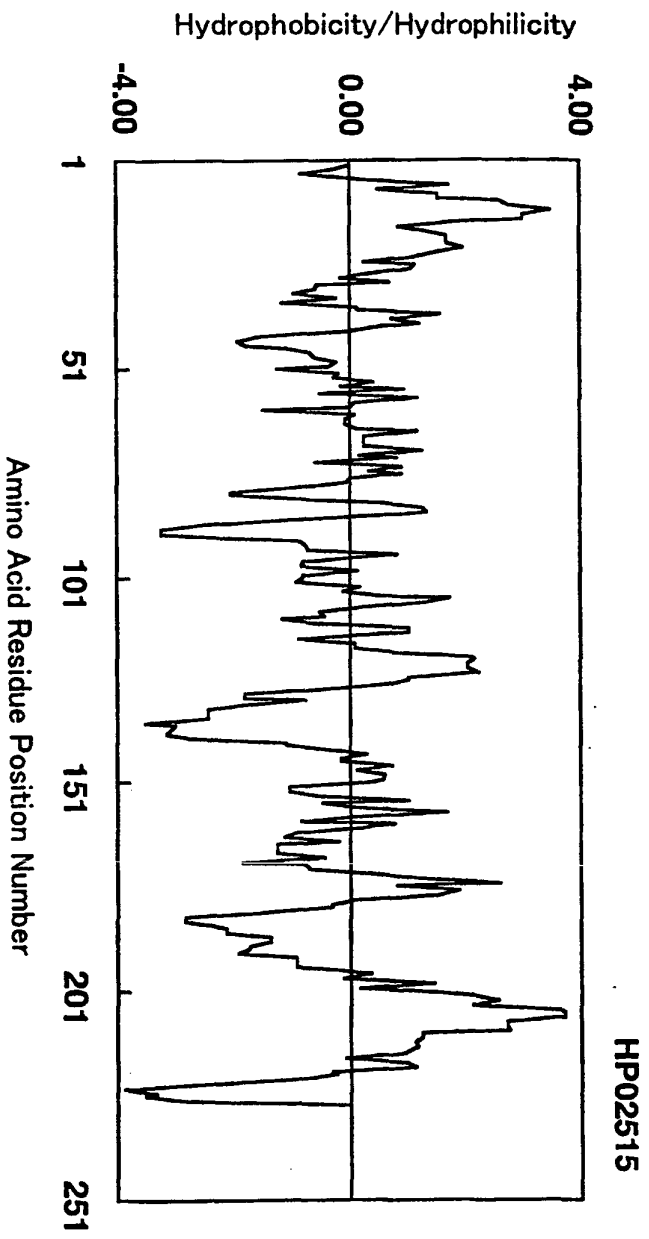


Fig.12

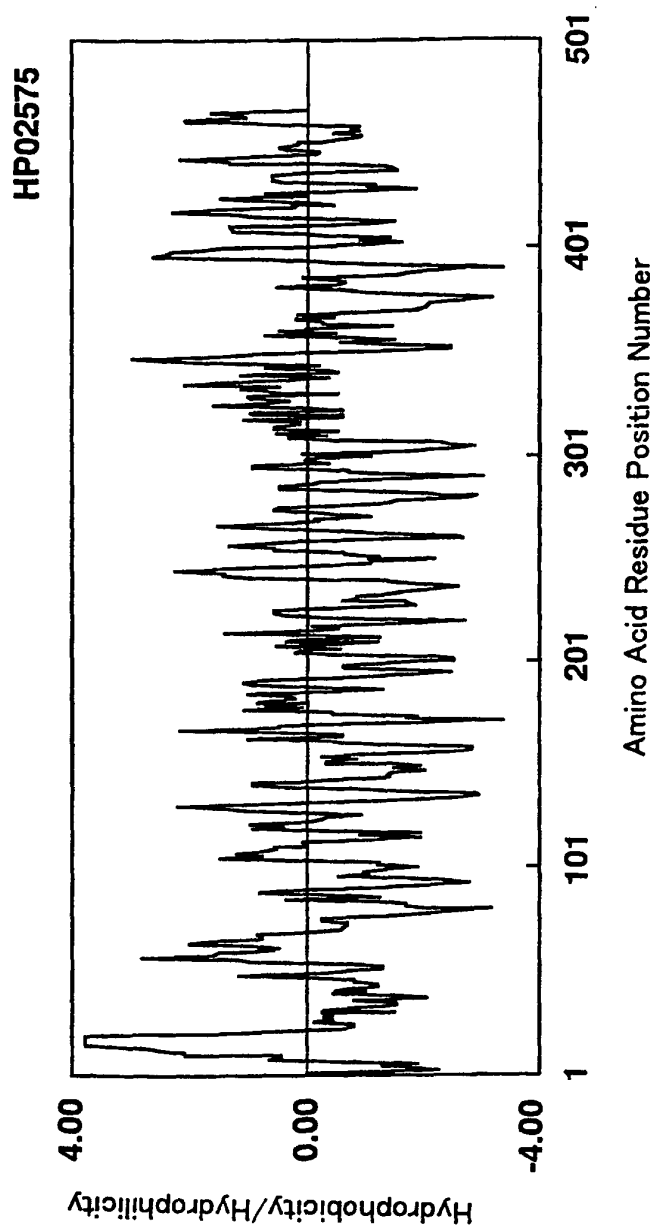


Fig. 13

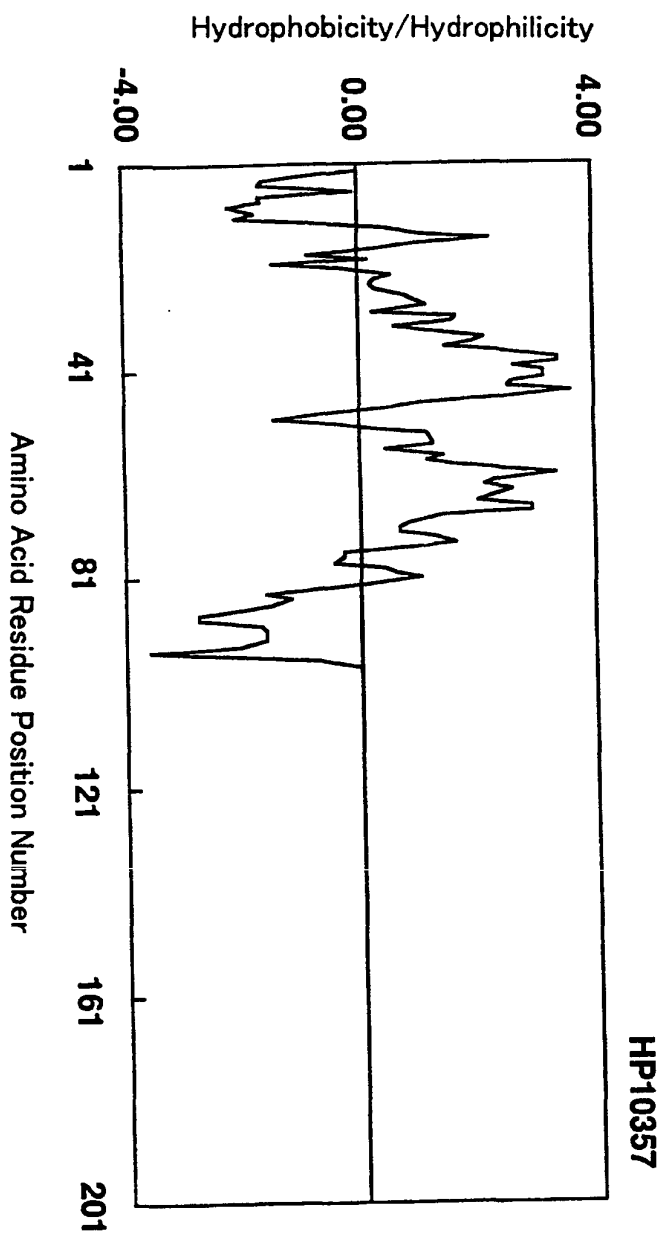


Fig. 14

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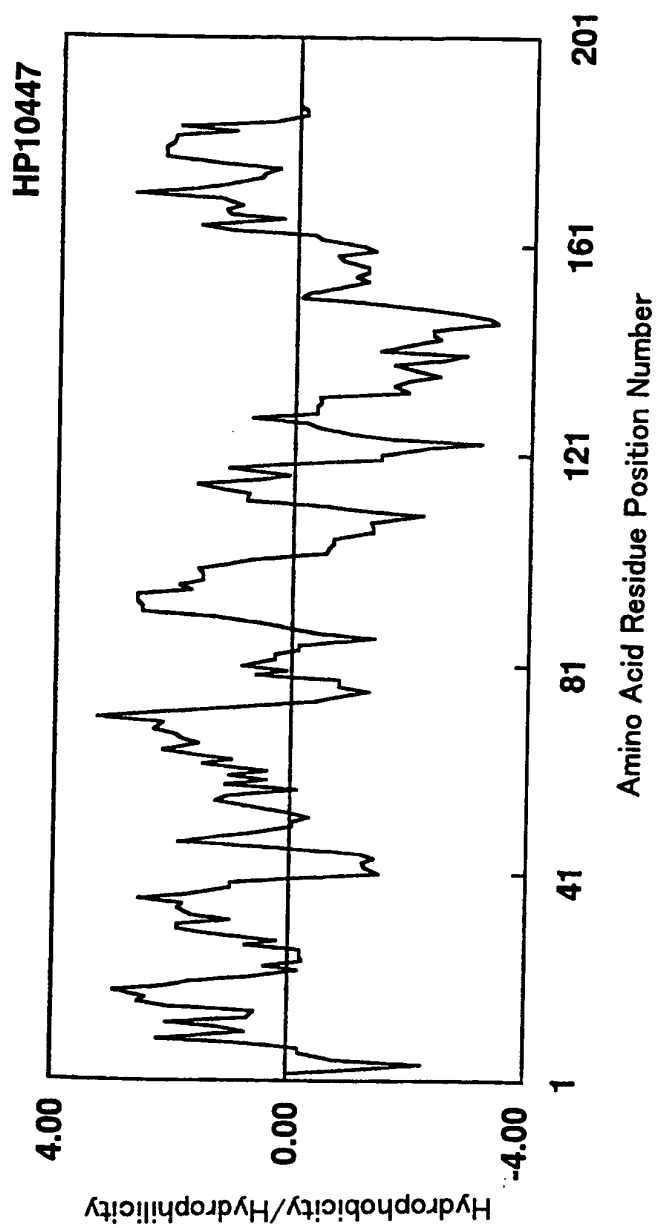


Fig. 15

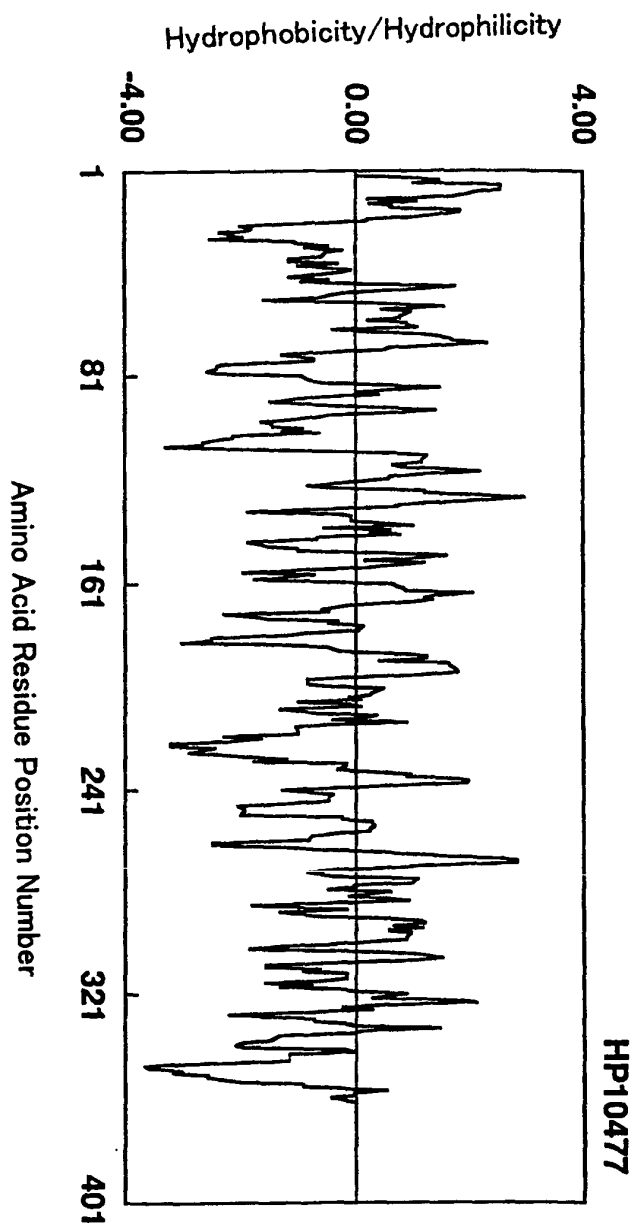


Fig. 16



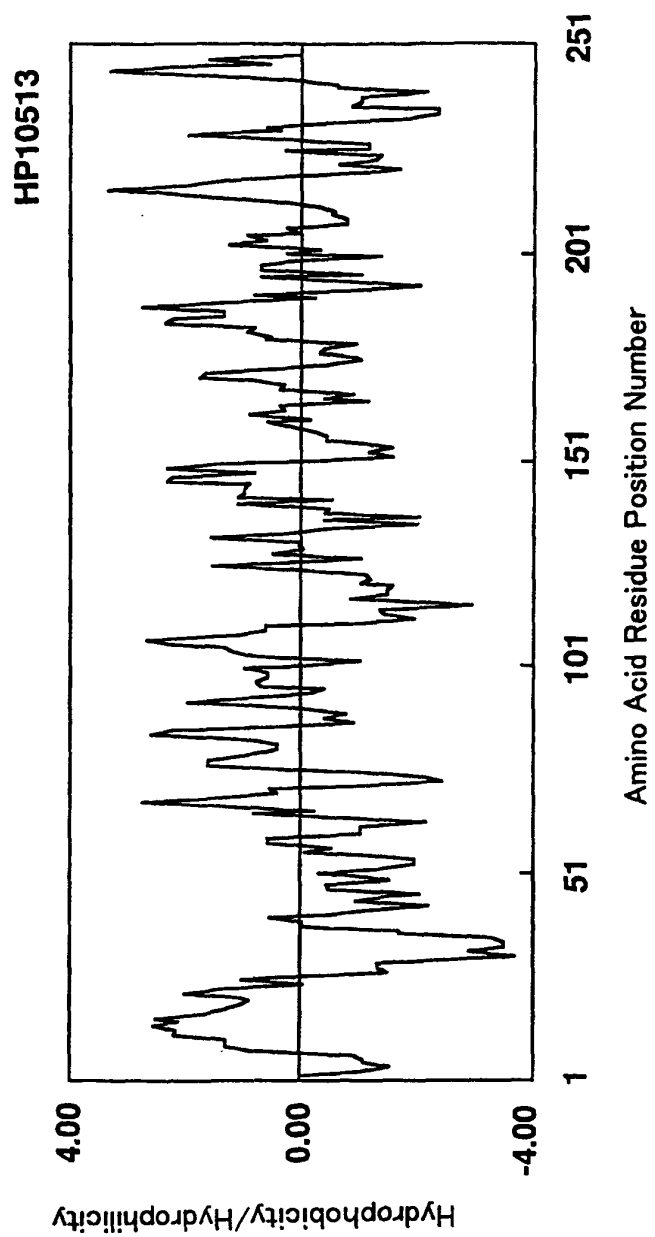


Fig.17

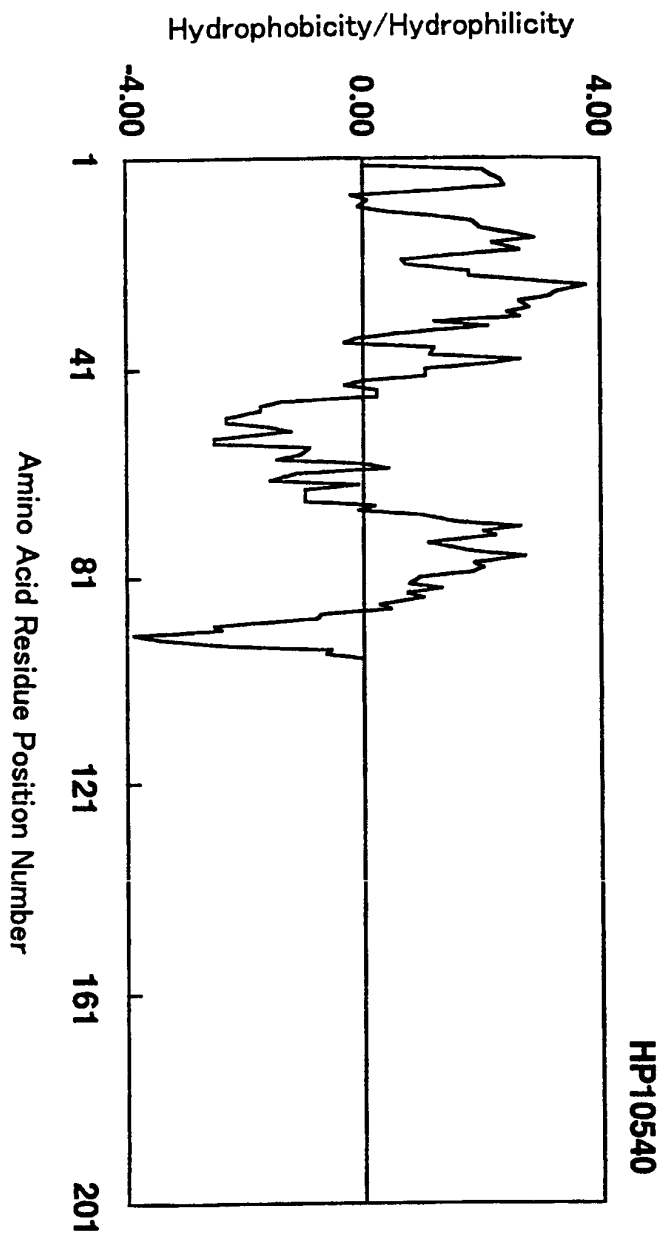


Fig. 18

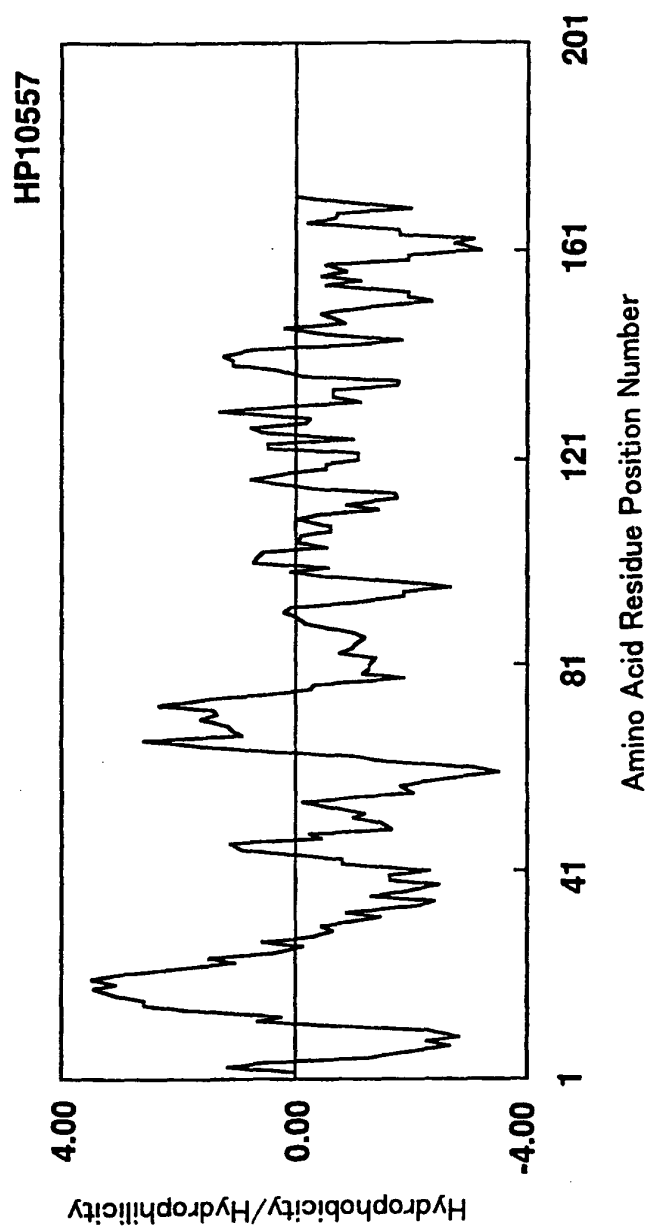


Fig. 19

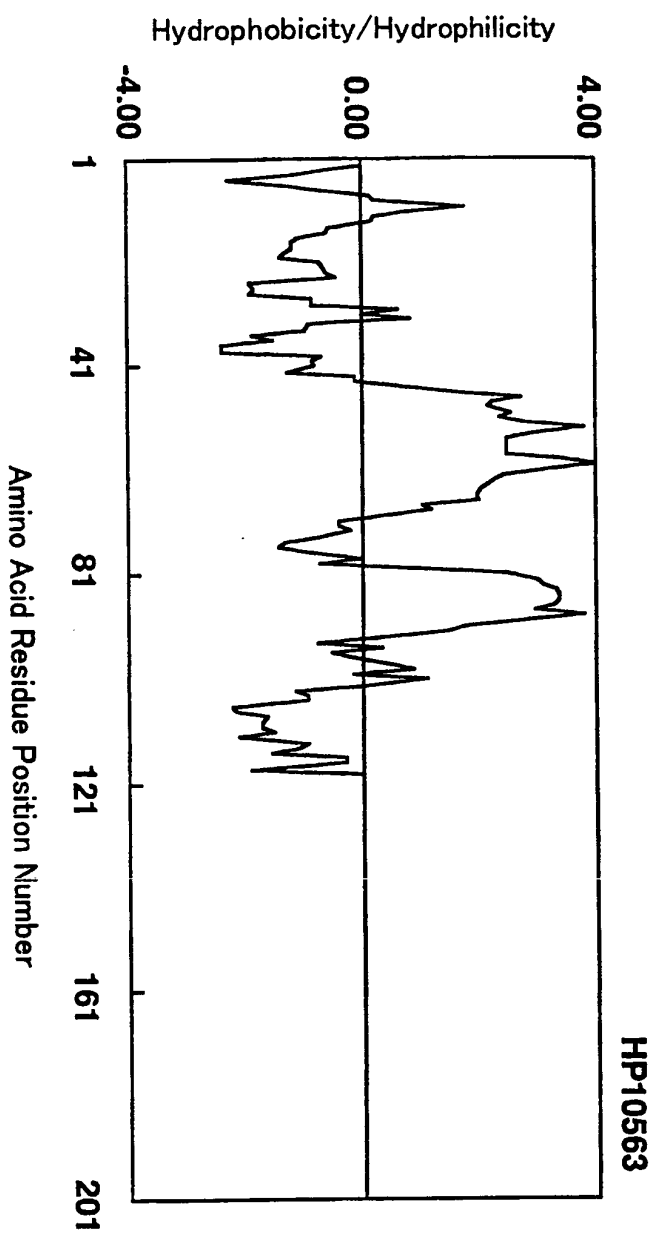


Fig. 20

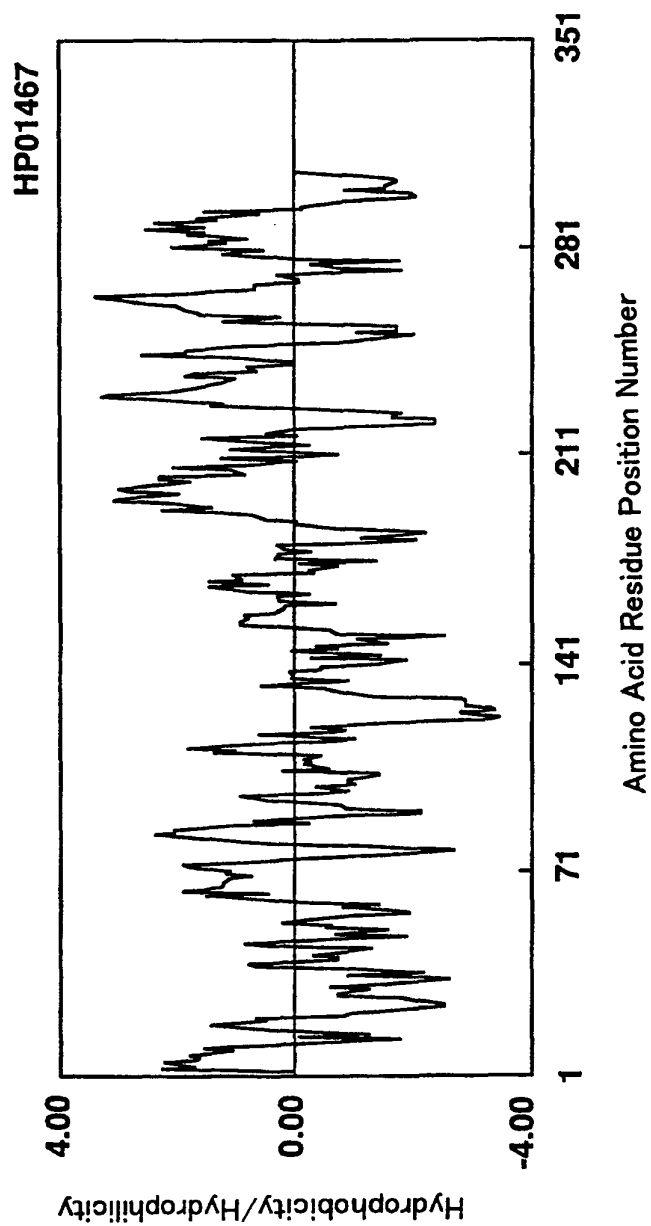


Fig. 21

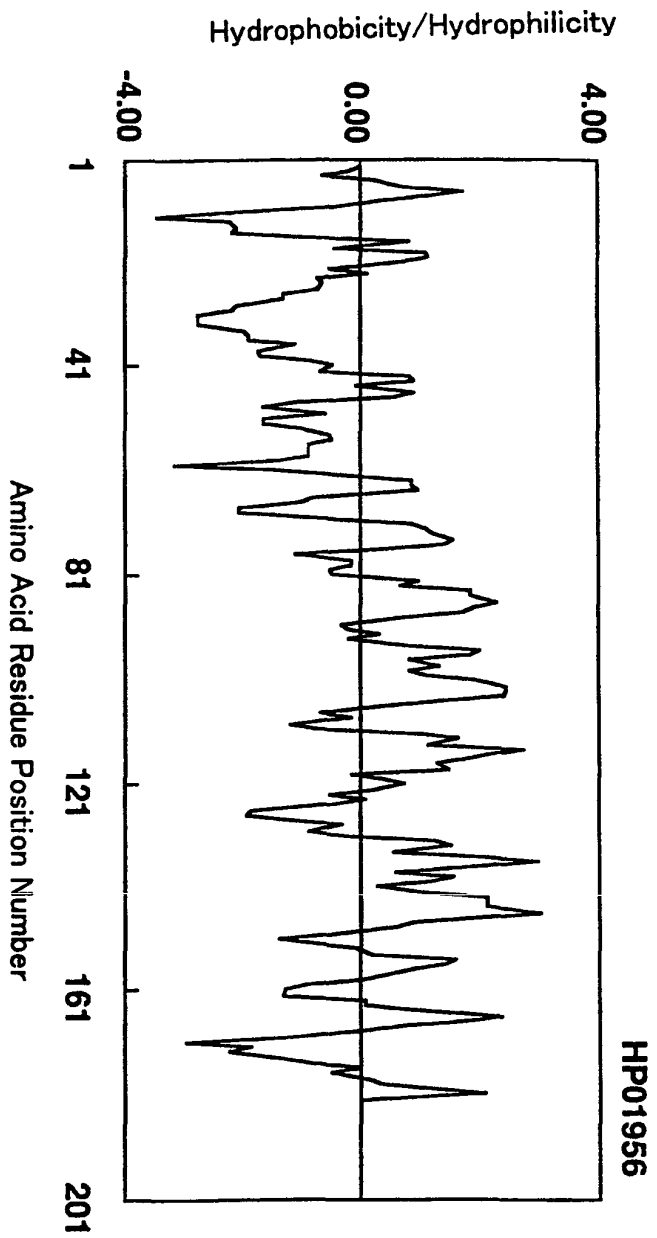


Fig.22

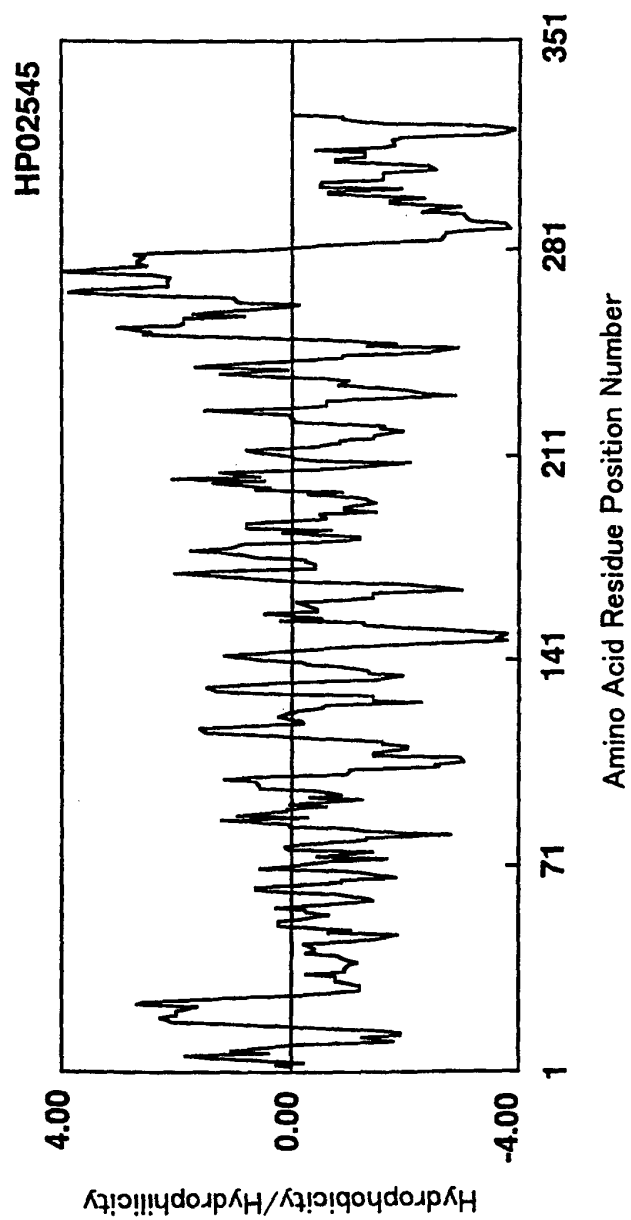


Fig. 23

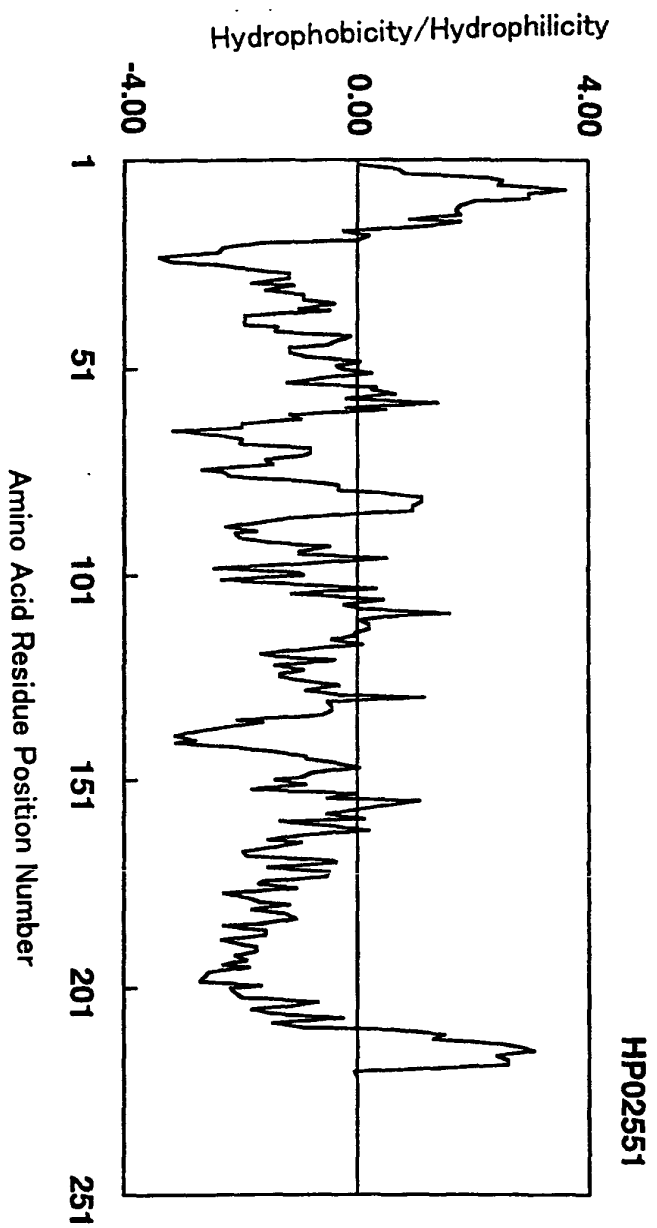


Fig. 24



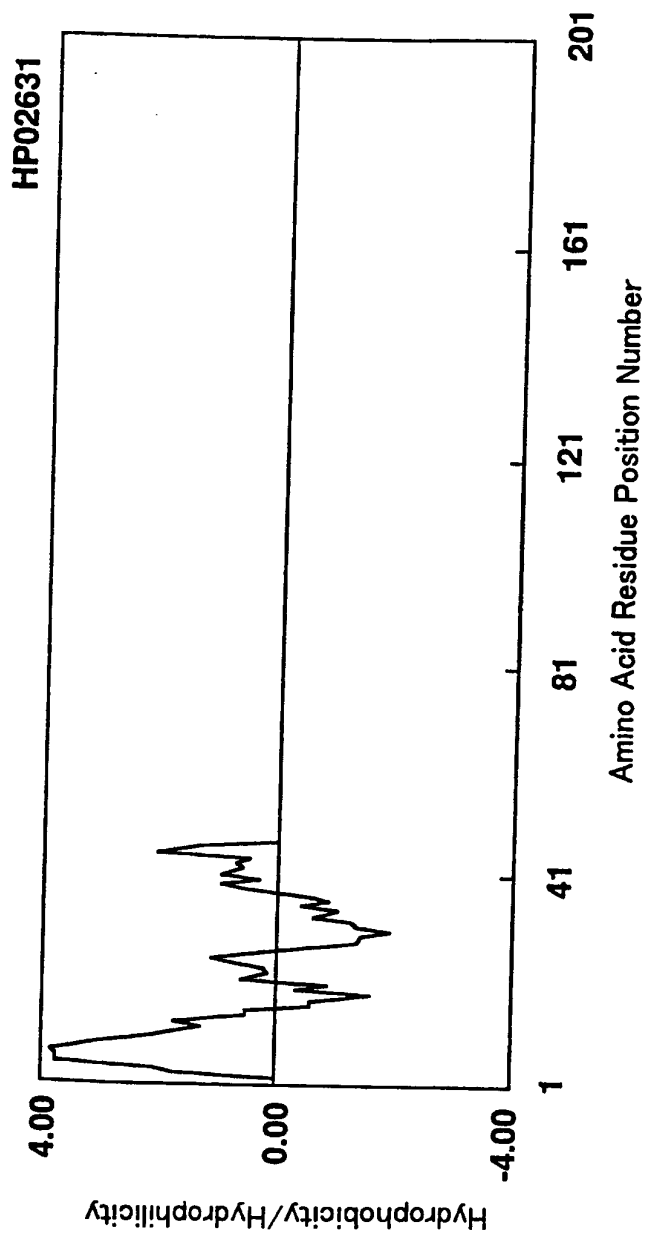


Fig. 25

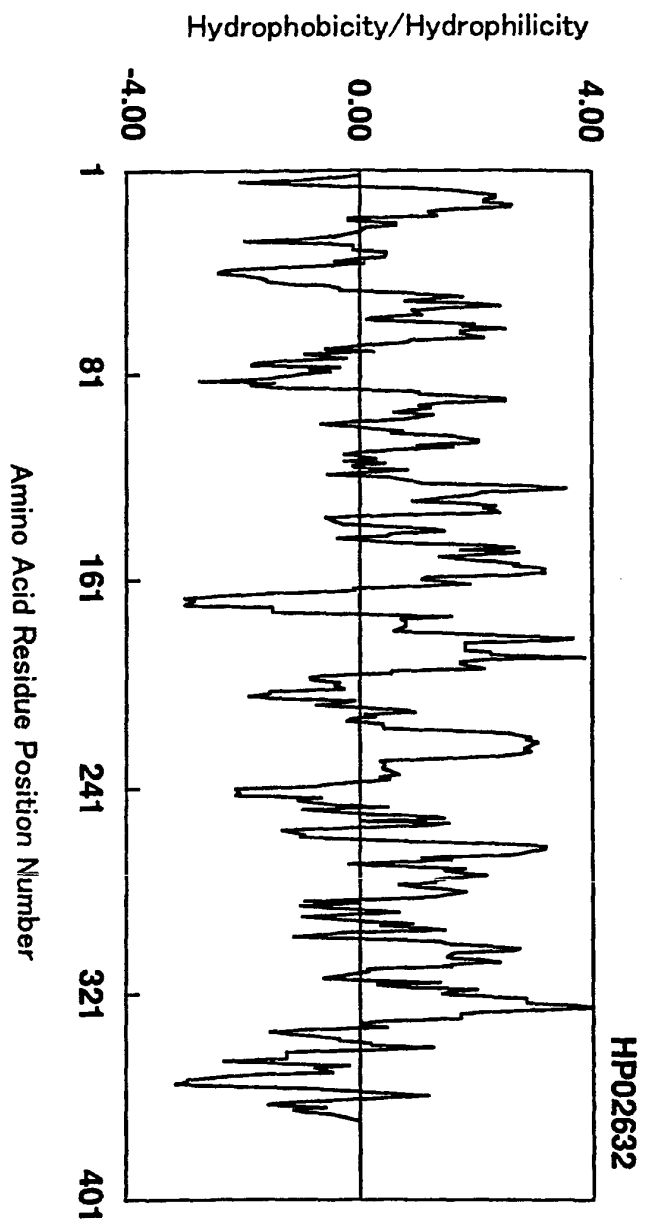


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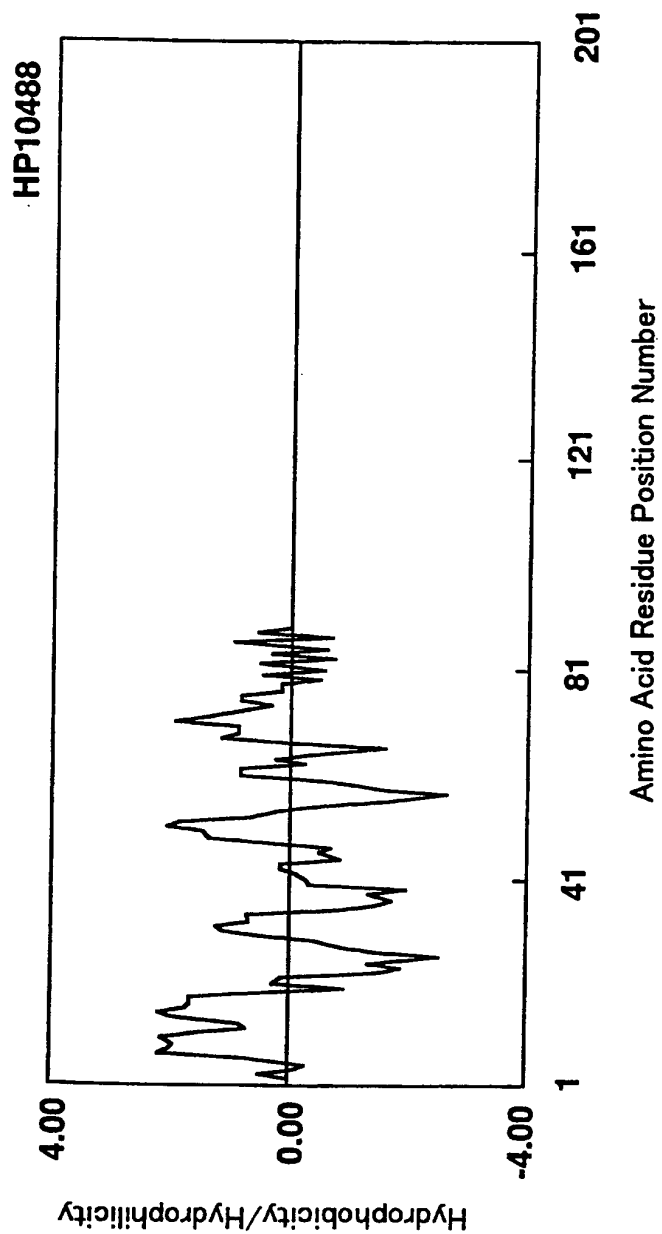


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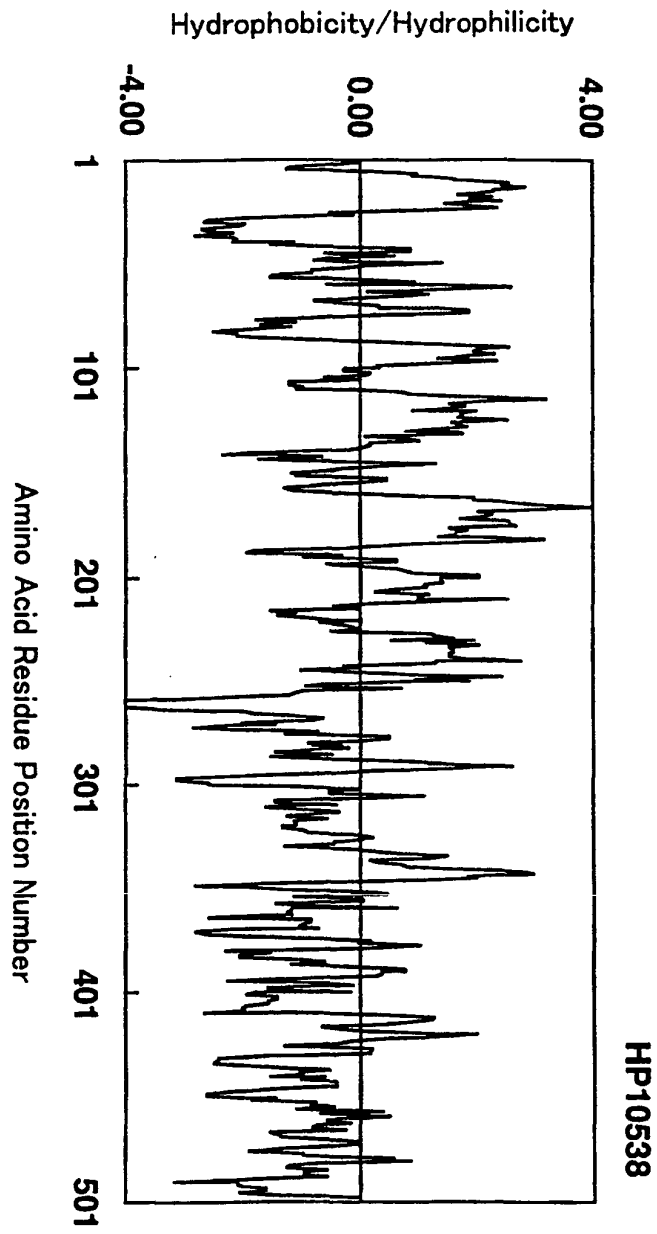


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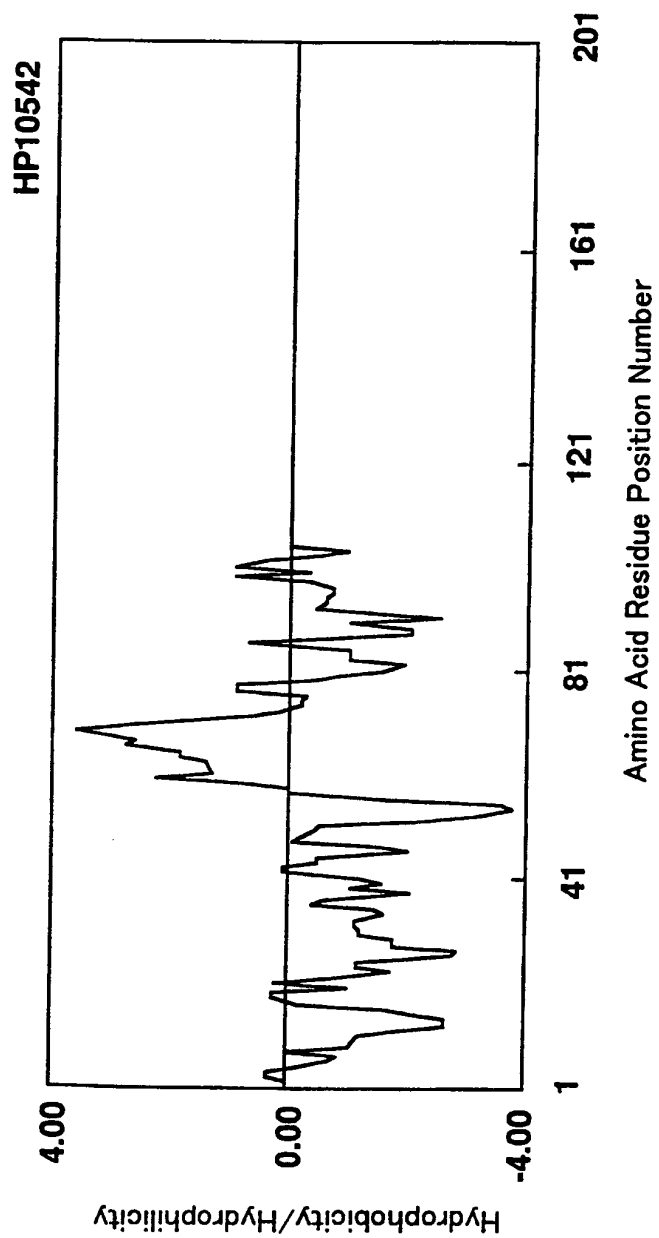
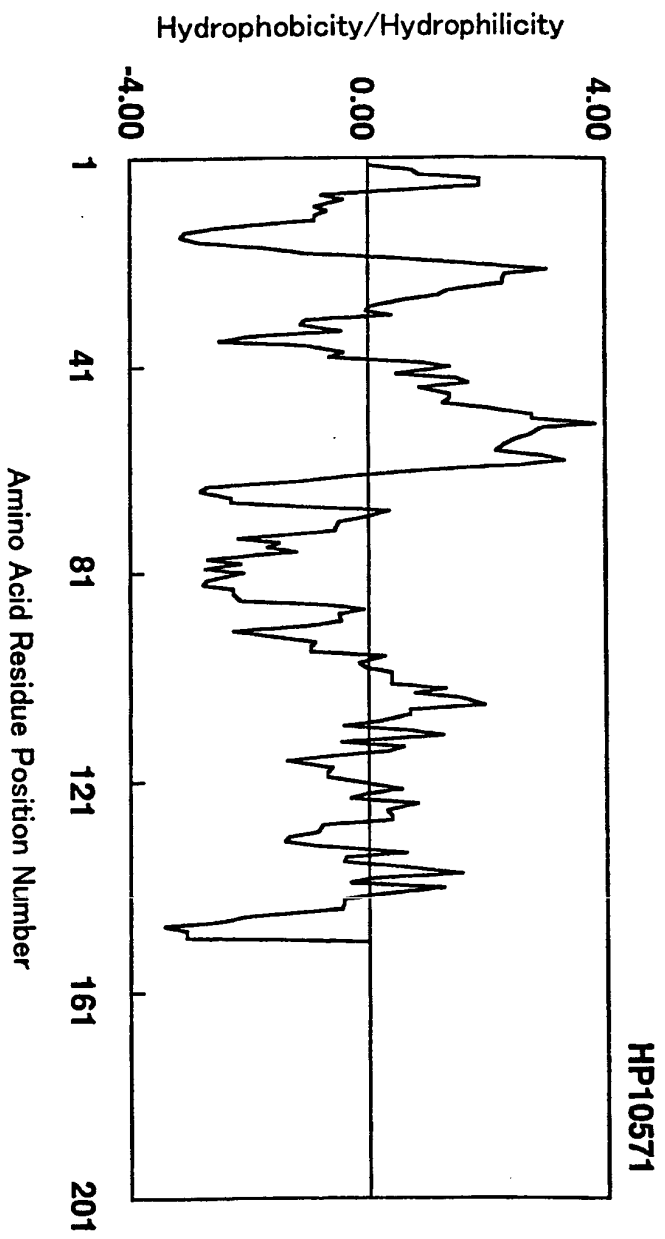


Fig. 29



**Fig. 30**

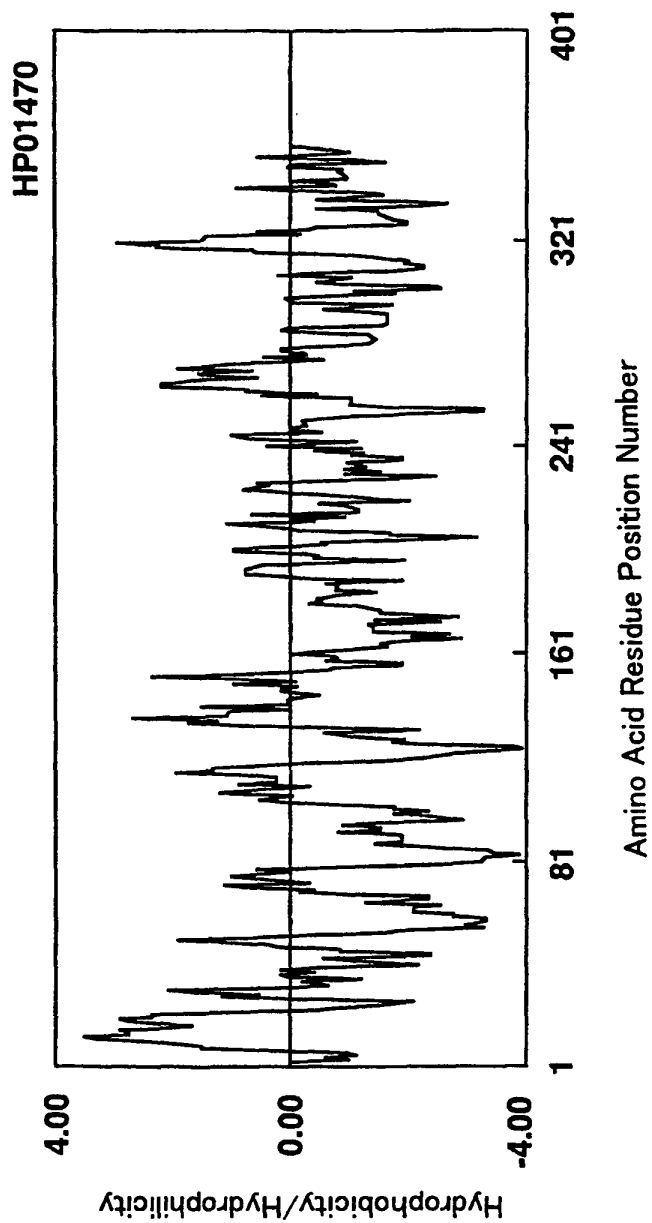


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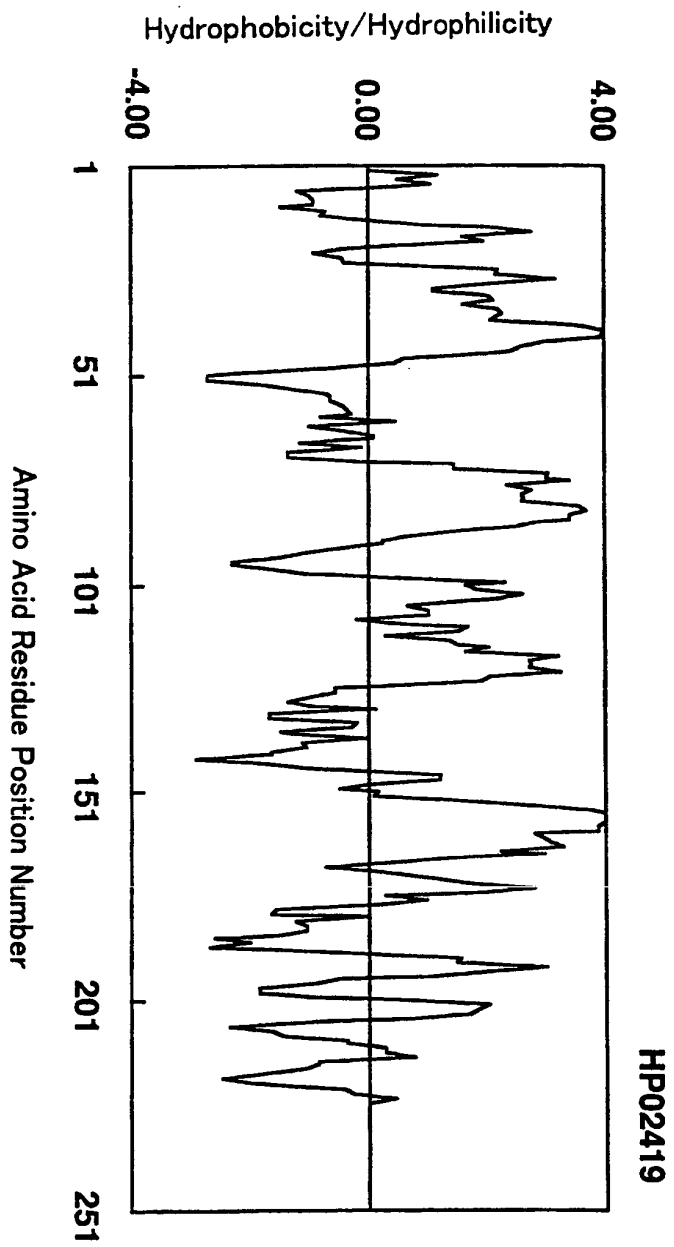


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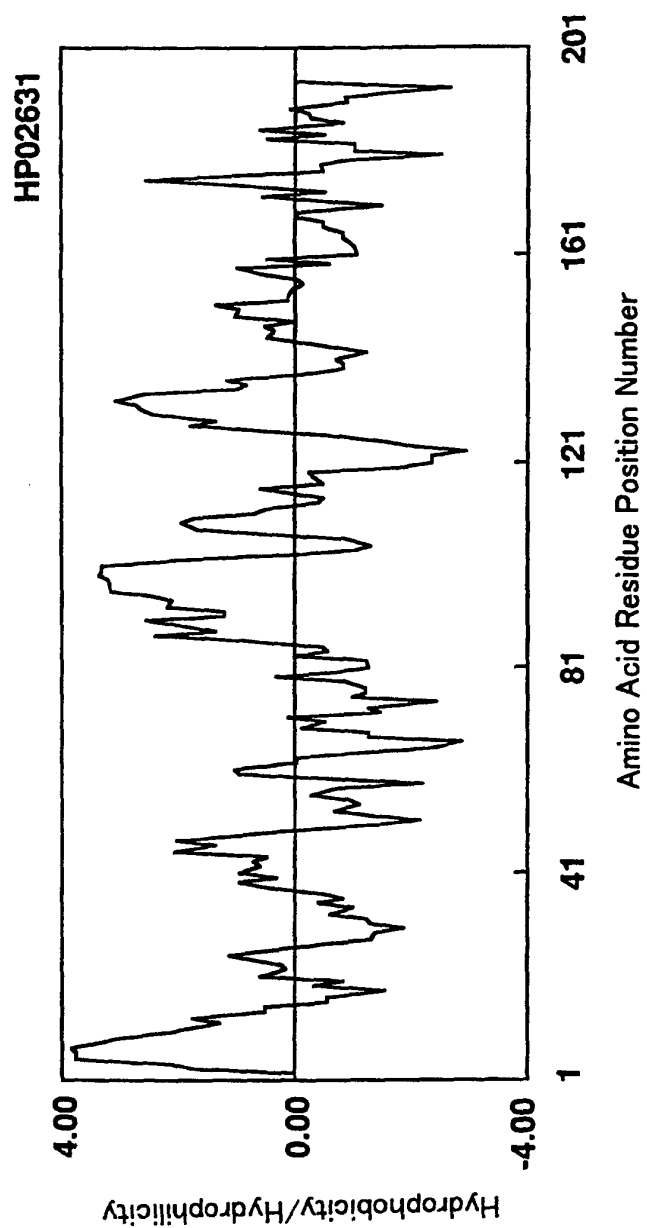


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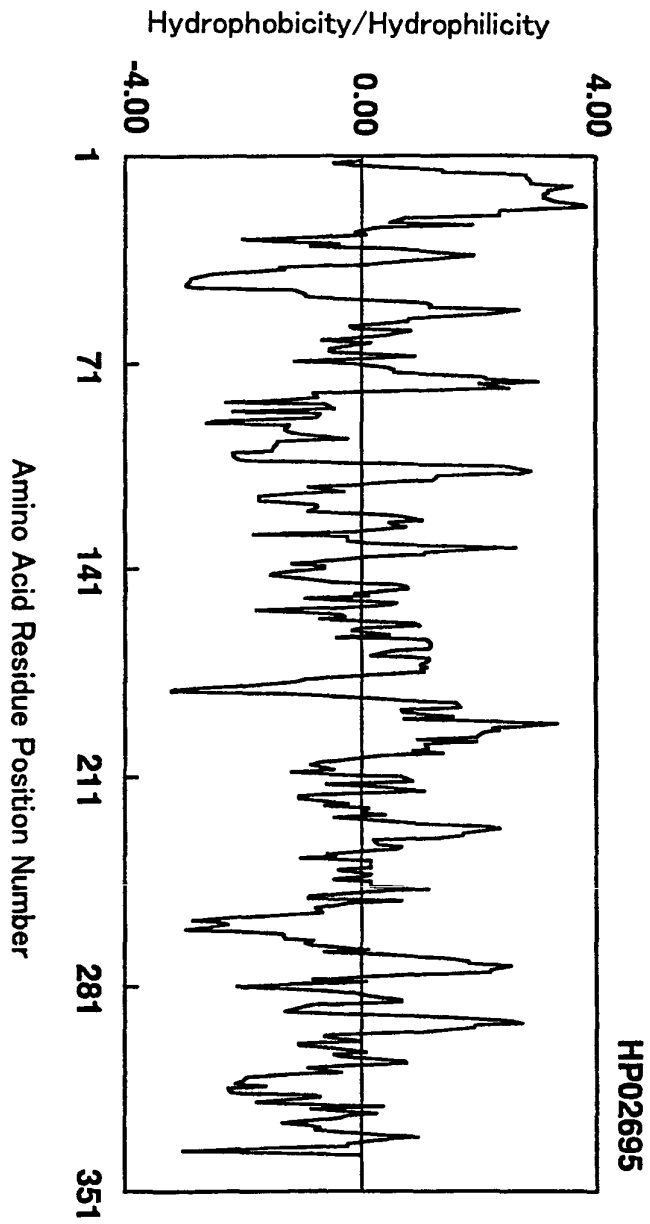


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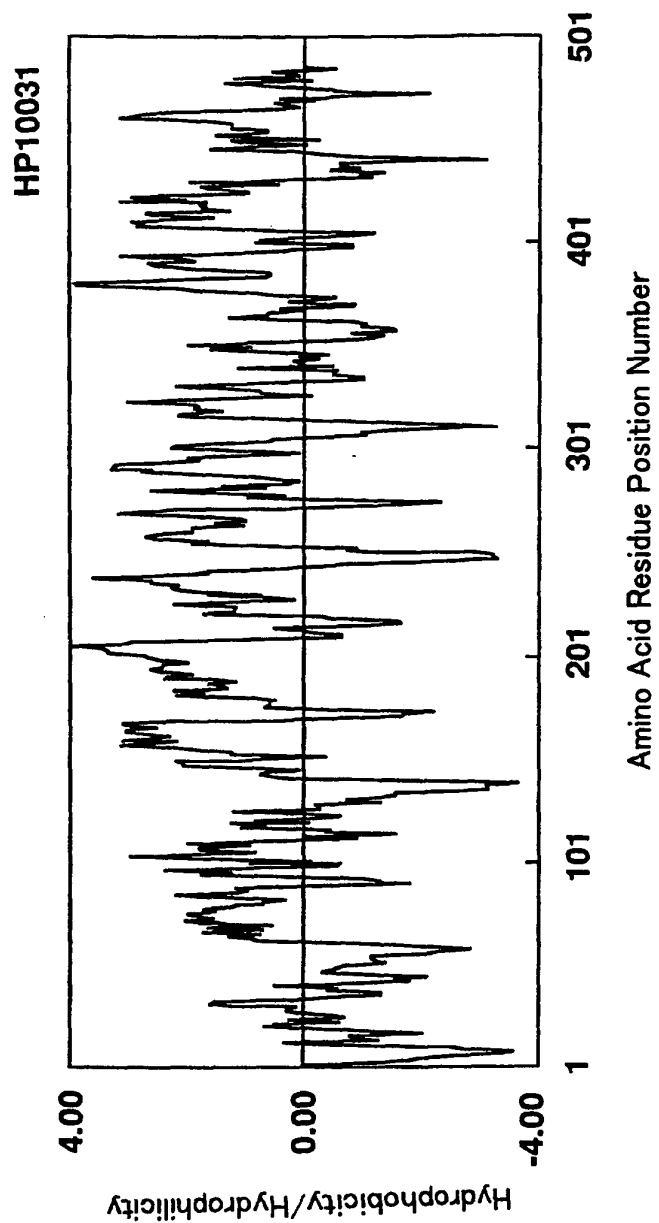


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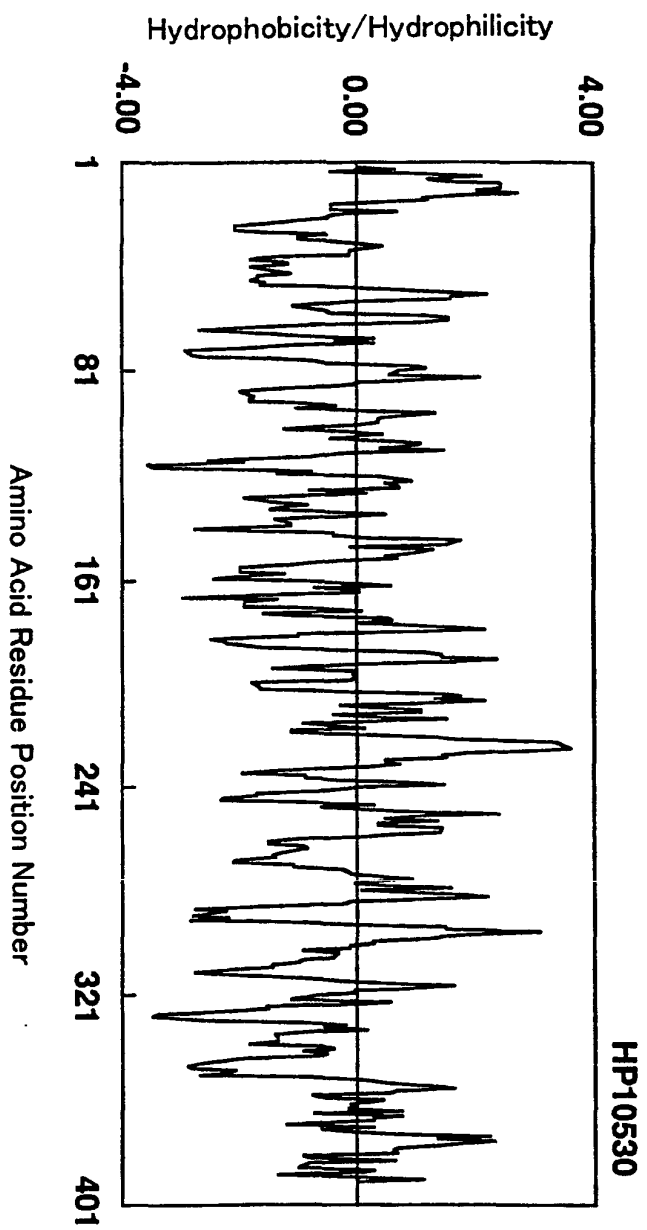


Fig. 36

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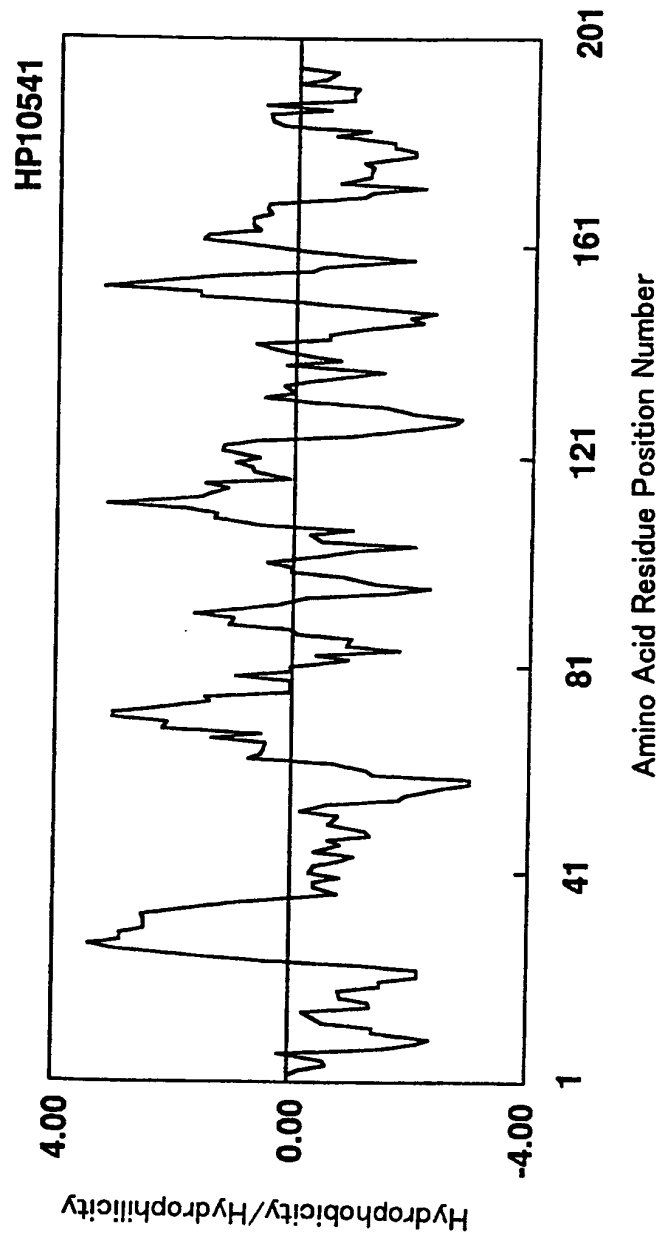


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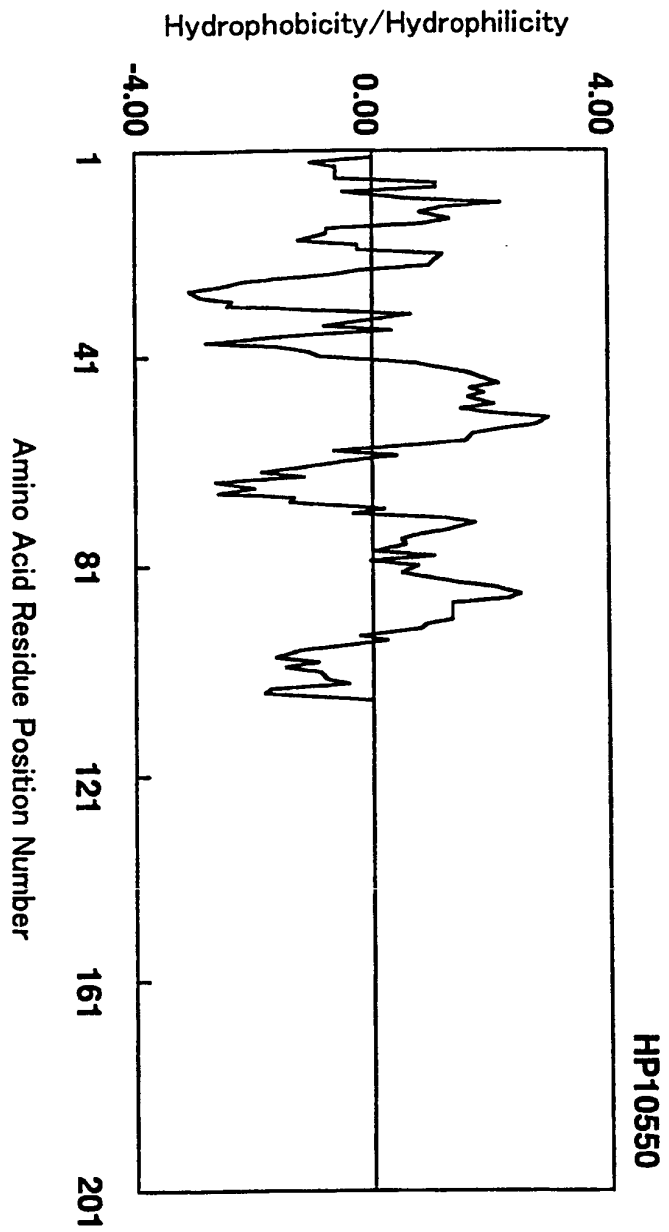


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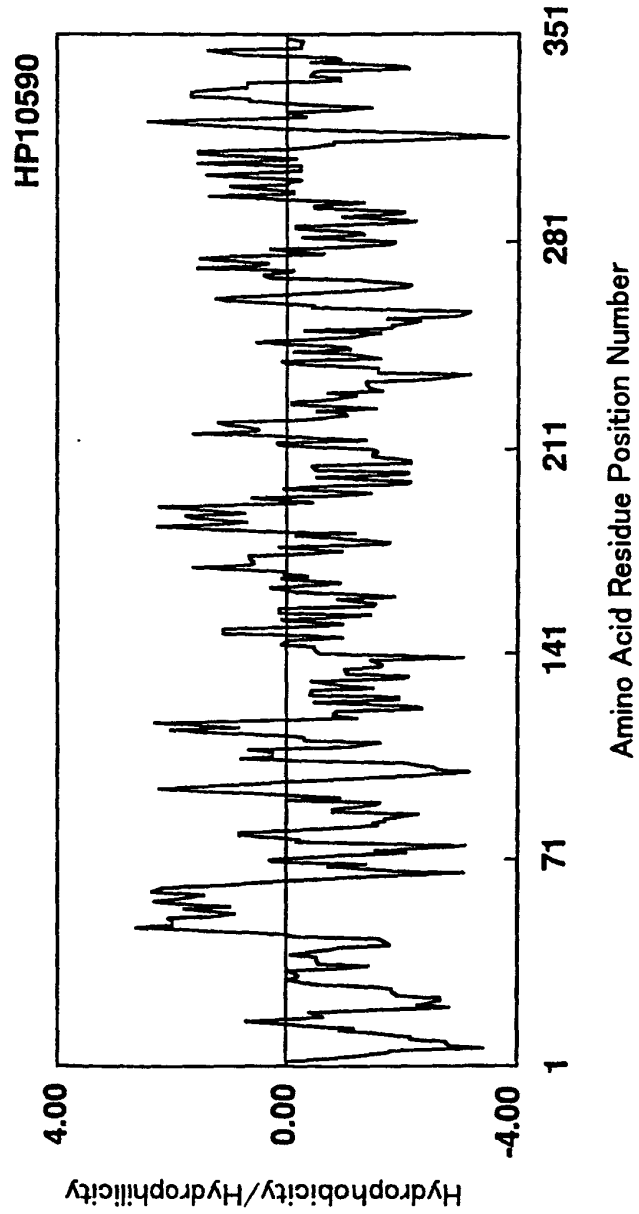


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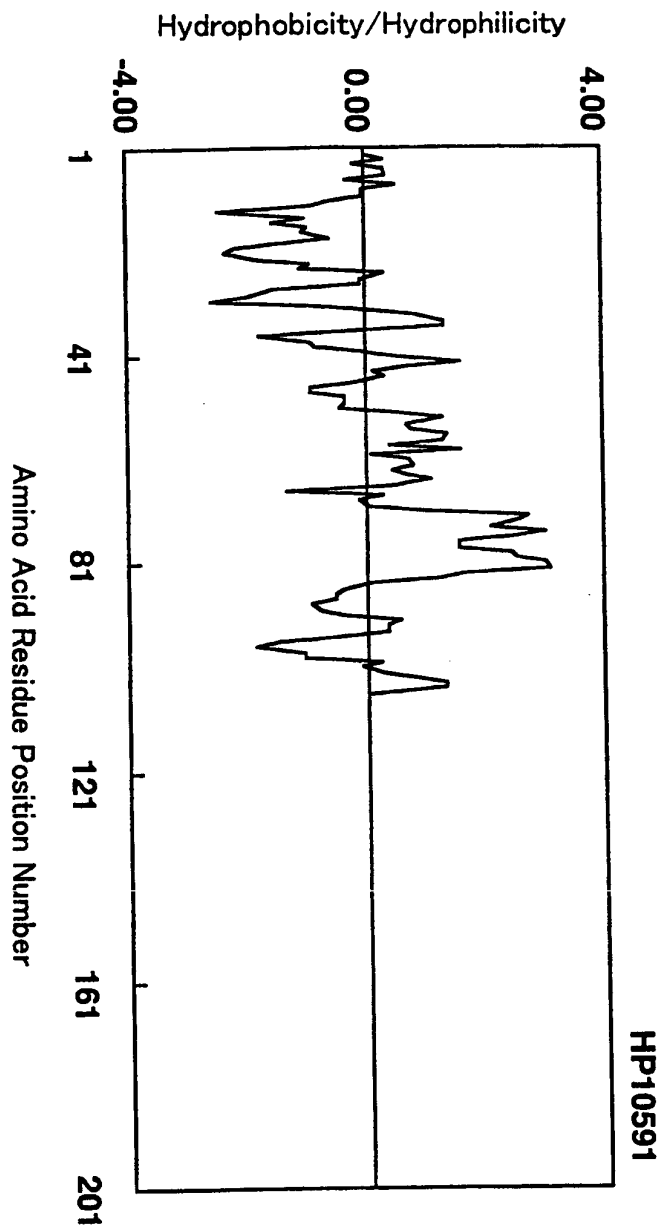


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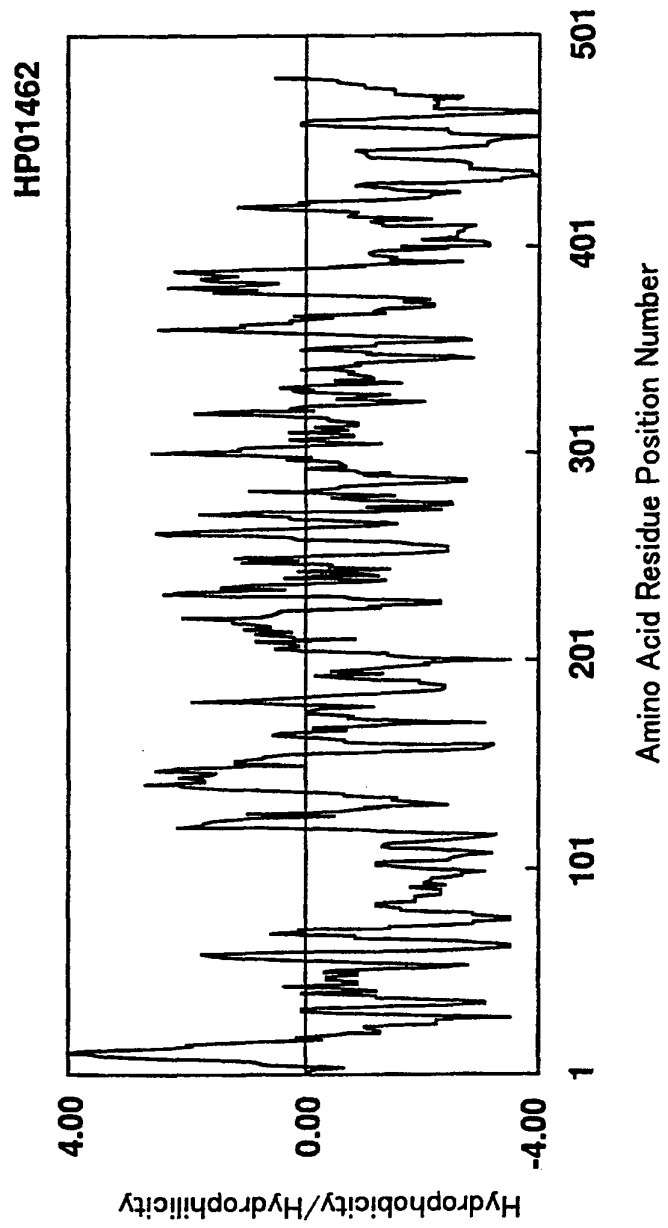


Fig. 41

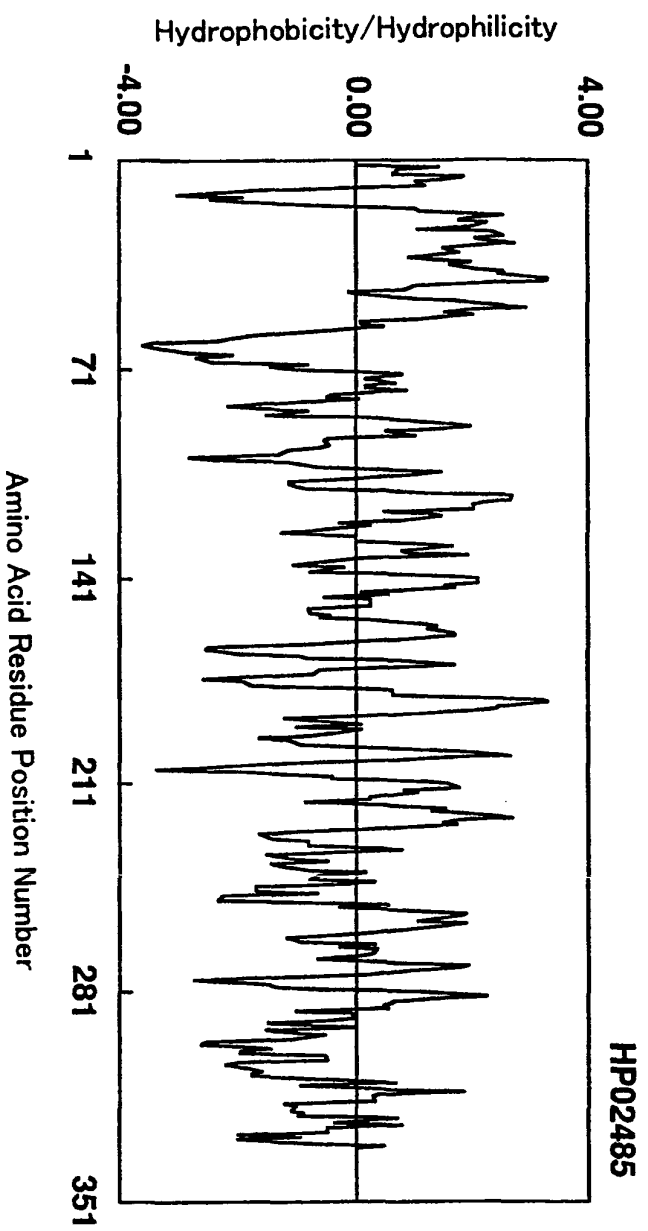


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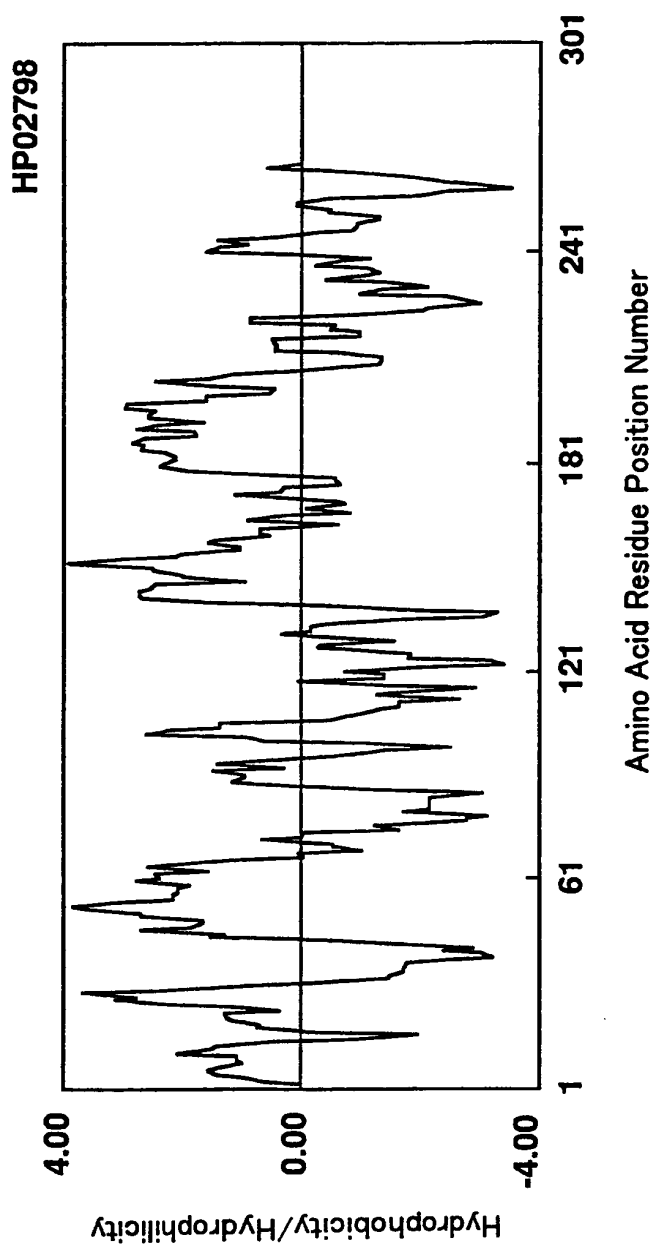


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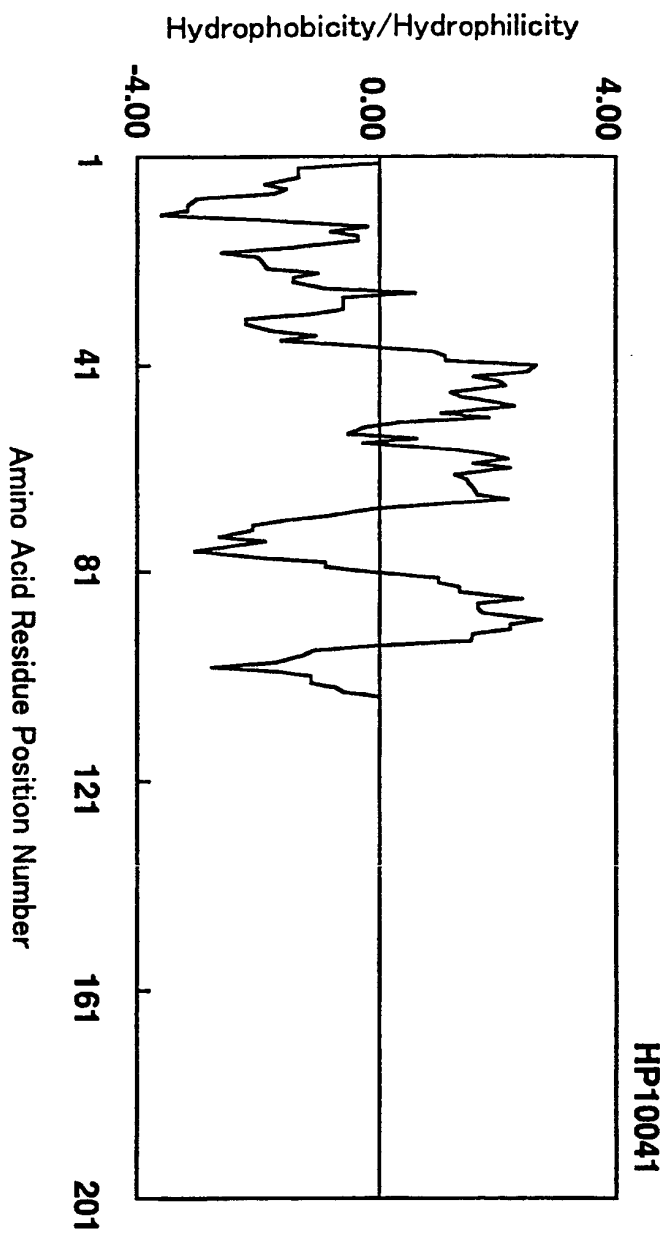


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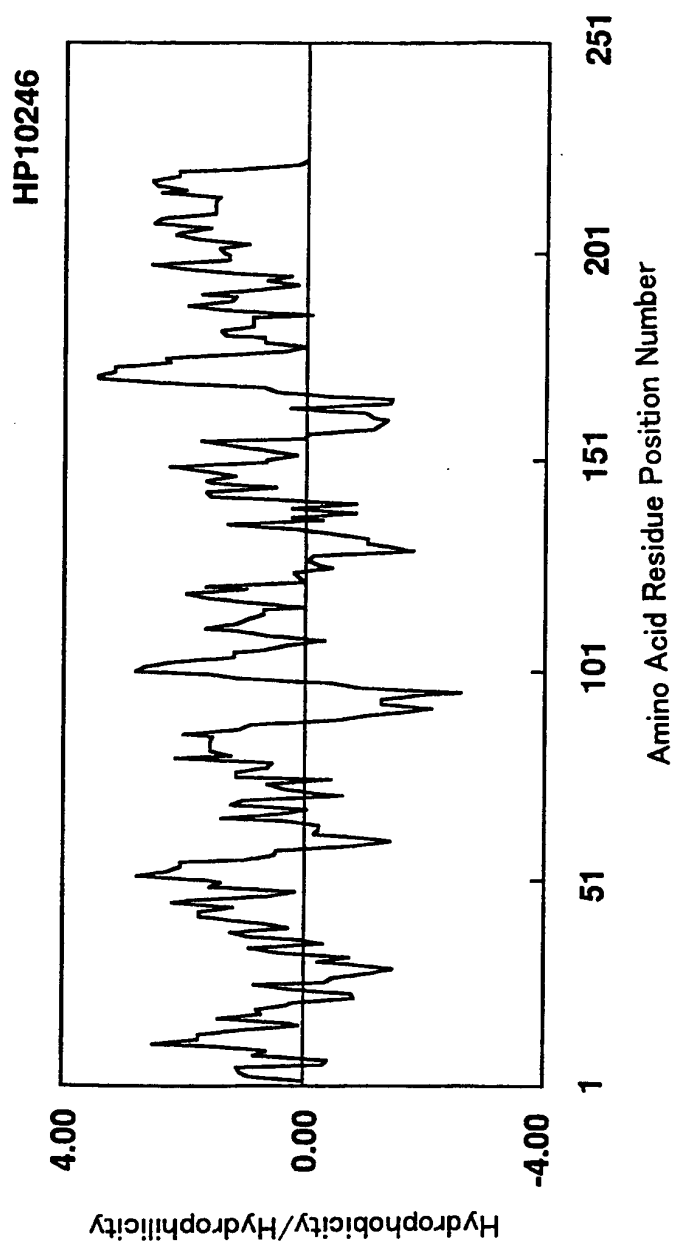


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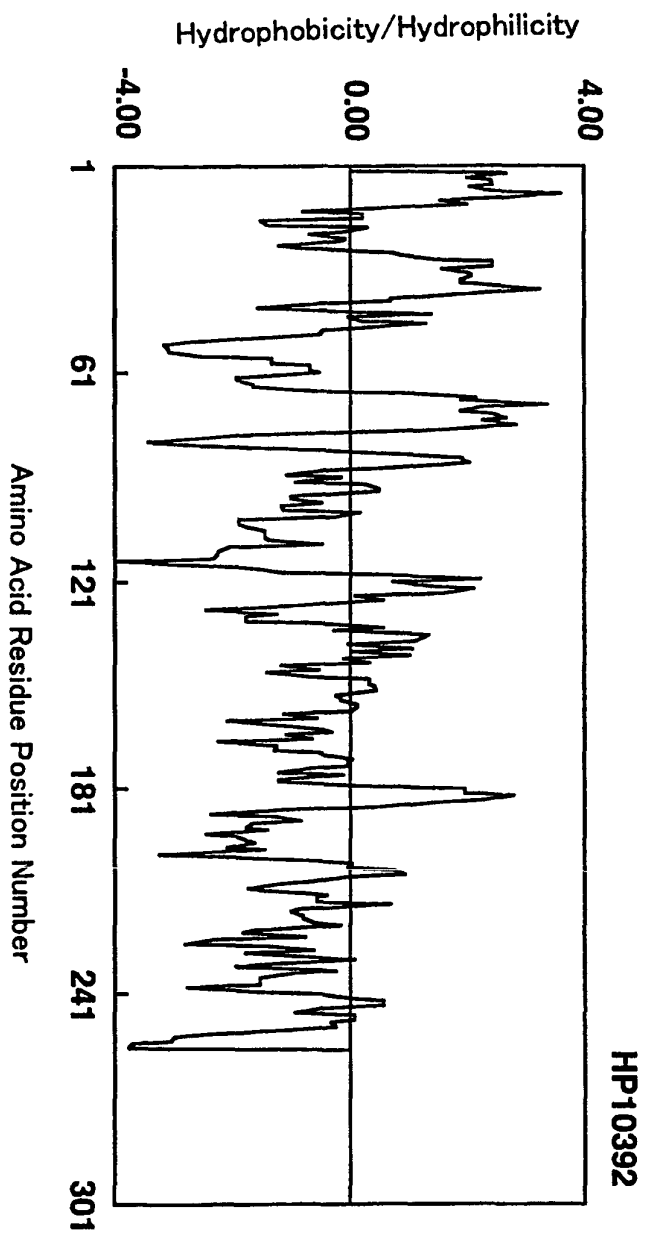


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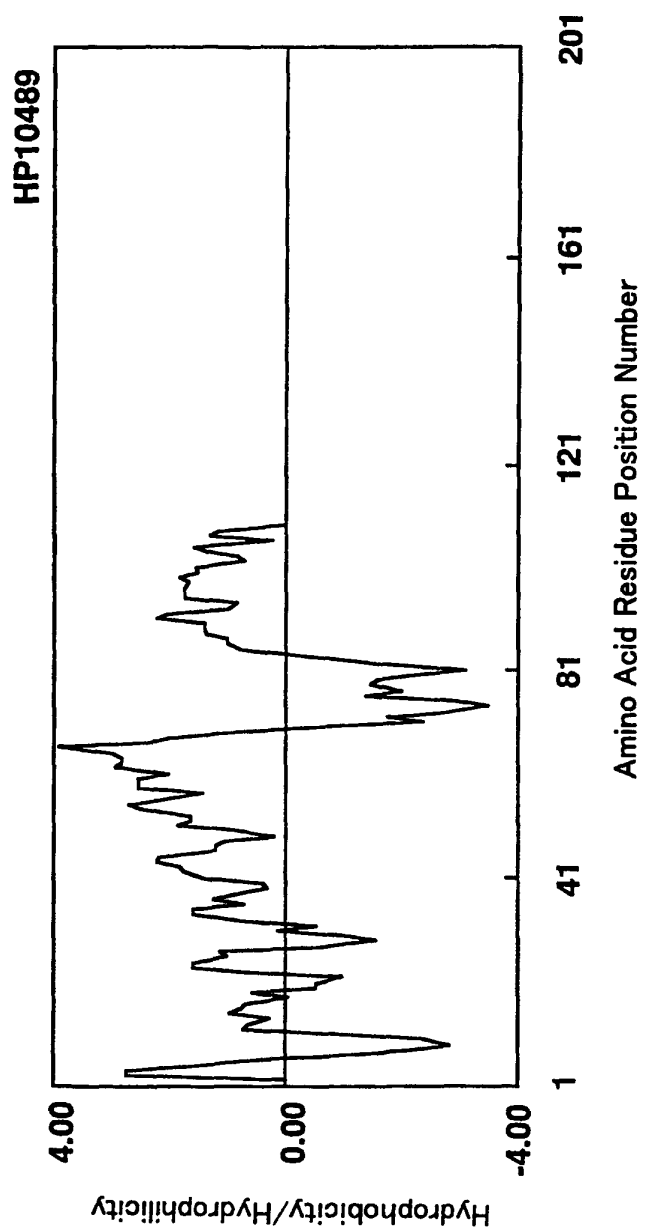


Fig.47

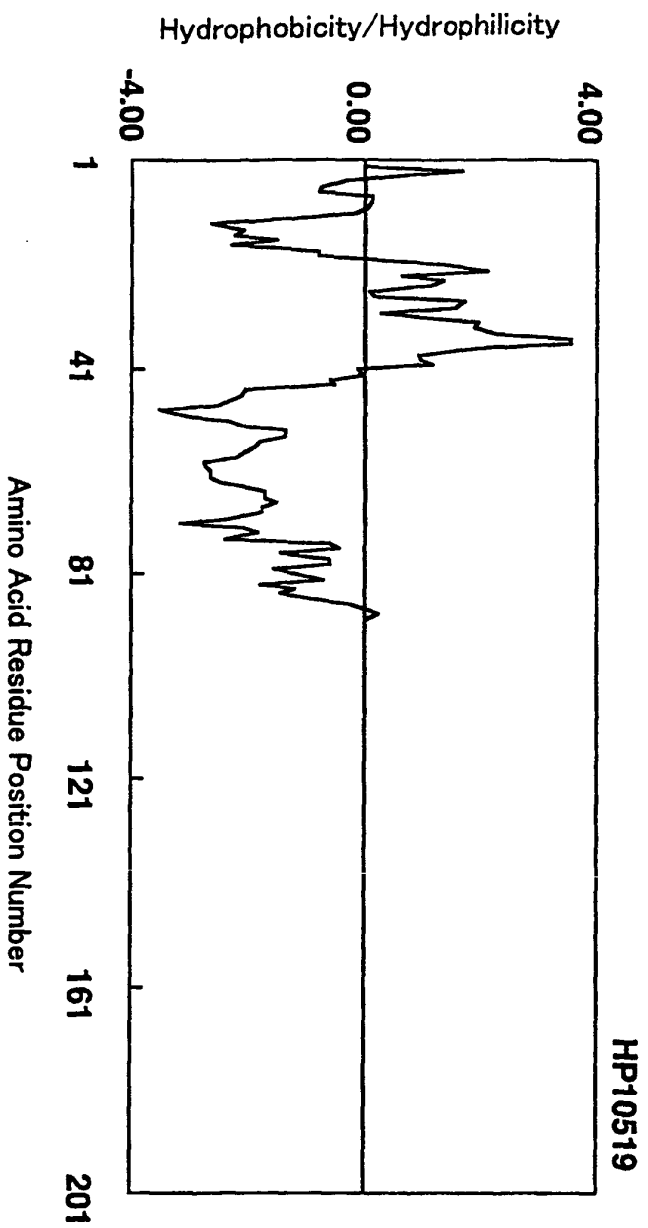


Fig. 48



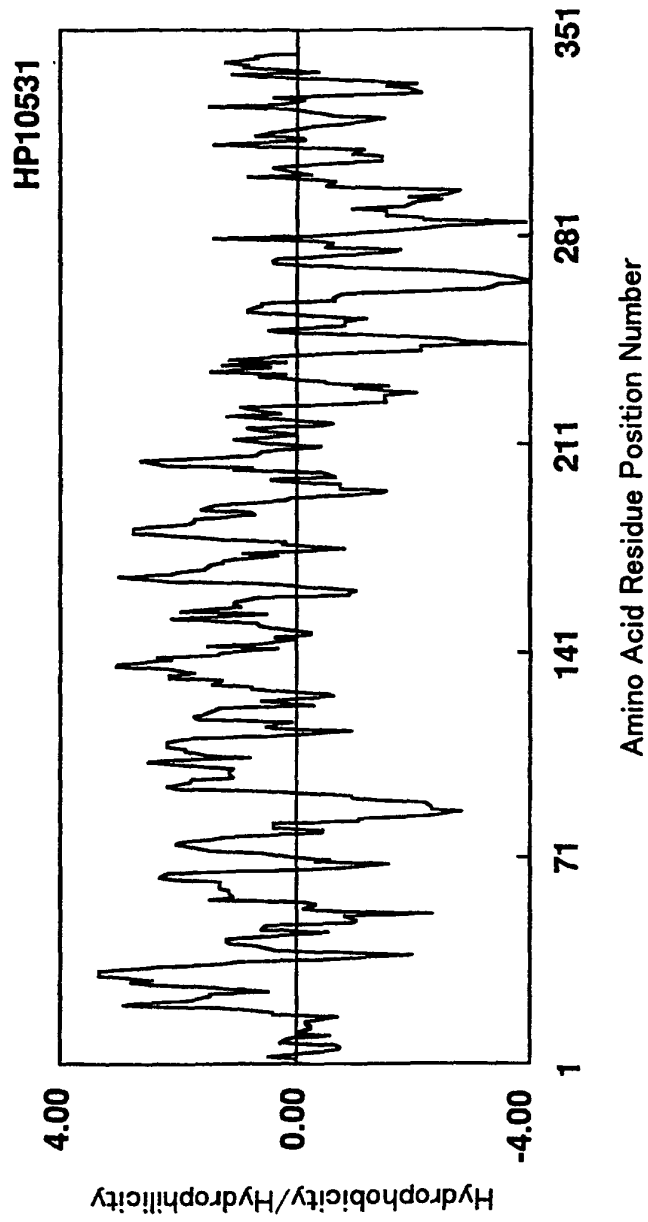


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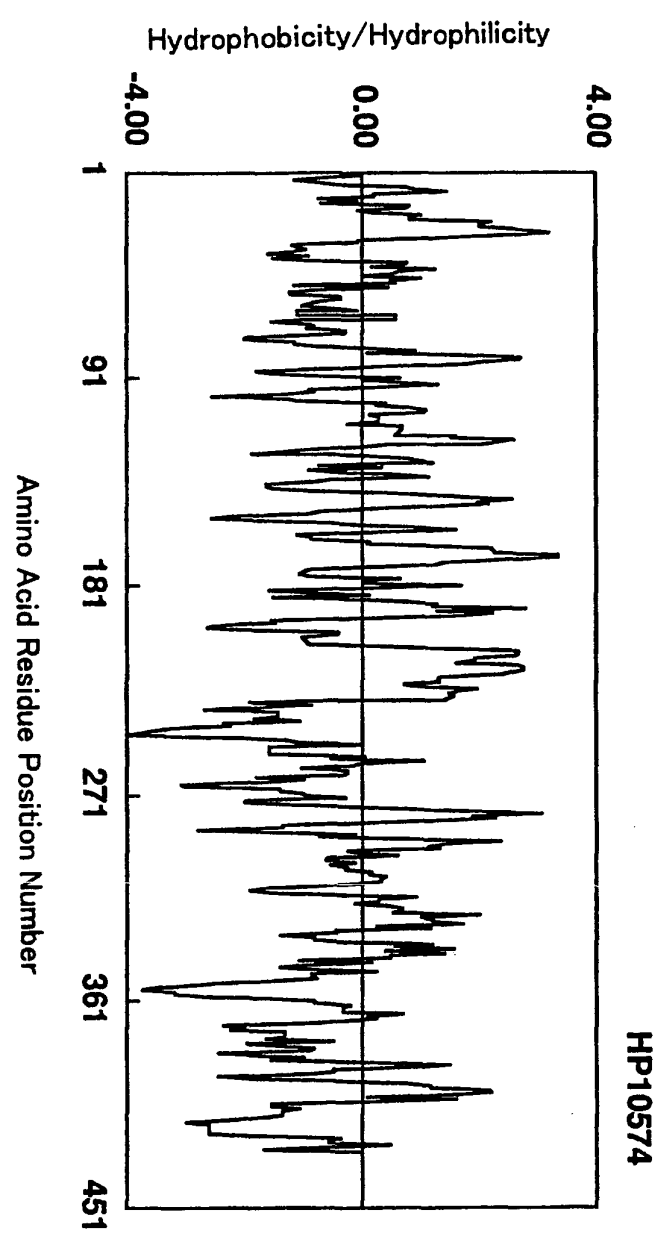


Fig. 50

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720 gttgaatcac tttaatggatg gcttcagata ctcacaacac ttagcgatga ccccaagta  
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	Lys Ala Leu Ile Ser Leu Ser Phe Gly Gly Ala Ile Gly Leu Met Phe	
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	ttg atg ctt gga tgt gcc ctt cca ata tac aac aaa tac tgg ccc ctc	211
	Leu Met Leu Gly Cys Ala Leu Pro Ile Tyr Asn Lys Tyr Trp Pro Leu	
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	ttt gtt cta ttt ttt tac atc ctt tca cct att cca tac tgc ata gca	259
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	aga aga tta gtg gat gat aca gat gct atg agt aac gct tgt aag gaa	307
	Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn Ala Cys Lys Glu	
	55 60 65	
20	ctt gcc atc ttt ctt aca acg ggc att gtc gtg tca gct ttt gga ctc	355
	Leu Ala Ile Phe Leu Thr Thr Gly Ile Val Val Ser Ala Phe Gly Leu	
	70 75 80	
	cct att gta ttt gcc aga gca cat ctg att gag tgg gga gct tgt gca	403
	Pro Ile Val Phe Ala Arg Ala His Leu Ile Glu Trp Gly Ala Cys Ala	
25	85 90 95 100	
	ctt gtt ctc aca gga aac aca gtc atc ttt gca act ata cta ggc ttt	451
	Leu Val Leu Thr Gly Asn Thr Val Ile Phe Ala Thr Ile Leu Gly Phe	
	105 110 115	
	ttc ttg gtc ttt gga agc aat gac gac ttc agc tgg cag cag tgg tgaa	500
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	caggagatgg ggcagttaat gctgaatggt atagcaagcc tcttggggggt attttaggtg	620
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	gccccgcctc tggcctgtct ctcgcatggc gtcgcctcca ggggcc atg gcg aag	295
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	His Gln Ile Leu Val Leu Asp Pro Thr Asp Leu Lys Phe Lys	
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	Gly Pro Phe Thr Asp Val Thr Thr Asp Leu Lys Leu Arg Asn Pro	
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	tcg gat aga aaa gtg tgt ttc aaa gtg aag act aca gca cct cgc cgg	35
	Ser Asp Arg Lys Val Cys Phe Lys Val Lys Thr Thr Ala Pro Arg Arg	40
	40	45
	50	
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	Tyr Cys Val Arg Pro Asn Ser Gly Ile Ile Asp Pro Gly Ser Thr Val	
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	Thr Val Ser Val Met Leu Gln Pro Phe Asp Tyr Asp Pro Asn Gln Lys	70
	70	75
	80	
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	Ser Lys His Lys Phe Met Val Gln Thr Ile Phe Ala Pro Pro Asn Thr	
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	gat tcc aaa ttg aga tgc gta ttt gaa atg ccc aat gaa aat gat aaa	679
5	Asp Ser Lys Leu Arg Cys Val Phe Glu Met Pro Asn Glu Asn Asp Lys	
	120 125 130	
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	135 140 145	
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	Glu Thr Arg Lys Leu Met Glu Glu Cys Lys Arg Leu Gln Gly Glu Met	
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	Met Lys Leu Ser Glu Glu Asn Arg His Leu Arg Asp Glu Gly Leu Arg	
	180 185 190 195	
	ctc aga aag gta gca cat tcg gat aaa cct gga tca acc tca act gca	919
20	Leu Arg Lys Val Ala His Ser Asp Lys Pro Gly Ser Thr Ser Thr Ala	
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	tcc ttc aga gat aat gtc acc agt cct ctt cct tca ctt ctt gtt gta	967
	Ser Phe Arg Asp Asn Val Thr Ser Pro Leu Pro Ser Leu Leu Val Val	
	215 220 225	
25	att gca gcc att ttc att gga ttc ttt cta ggg aaa ttc atc ttg	1012
	Ile Ala Ala Ile Phe Ile Gly Phe Phe Leu Gly Lys Phe Ile Leu	
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ttg cct tca aga aag ctg gct cta cag tta aga tcc att ttt att 349

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95

aag tat aaa tca aag cca ttc tgt gaa aaa ctg ctt tcc tgg gttg aaa 397

35

100

105

110

Lys Tyr Lys Ser Lys Pro Phe Cys Glu Lys Leu Leu Ser Trp Val Lys

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5	Gln Arg Asn Asp Leu Gln Leu Arg Ser Thr Pro Phe Arg Tyr Leu Leu	
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	aca cct tcc atg caa aaa agt gtt caa aat aaa ata aag agc ctt aac	541
	Thr Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn	
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10	tgg gaa gaa atg gaa aaa agc cgg tgc att cct gaa ata gat gat tcc	589
	Trp Glu Glu Met Glu Lys Ser Arg Cys Ile Pro Glu Ile Asp Asp Ser	
	160 165 170 175	
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	Glu Phe Cys Ile Arg Ile Pro Gly Gly Gly Ile Thr Lys Thr Leu Tyr	
15	180 185 190	
	gat gaa agc tgt tct aaa gaa atc caa atg gca gtt ctg ctg aaa ttt	685
	Asp Glu Ser Cys Ser Lys Glu Ile Gln Met Ala Val Leu Leu Lys Phe	
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	Leu Asn Glu Trp Leu Gln Ile Leu Lys Pro Leu Ser Asp Asp Pro Thr	
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	Gly Ser Gly Leu Pro Pro Ala Leu Phe	
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	910	tagtacaatt ccaacctgt atcctggctc tttagagacc taccacagac agtgaaagt			
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		100 105 110			
		Ala Leu Met Glu Gln Arg Leu Phe Trp Lys Phe Glu Gly Ala Val Val			
5	754	gct tgc atg gaa caa cgc tta ttt tgg aag ttc gaa ggg gct gtc gtc			
		85 90 95			
		Ile Thr Cys Ser Ser Ser Lys Arg Asn Glu Phe Lys Ser Cys Arg Ser			
	706	atc aca tgc agc tca tct aag aga atc gag ttc aaa agc tgc cgc tca			
		70 75 80			

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	Phe Tyr Leu Ala Ser Val Leu Met Gly Leu Val Leu Ile Cys Val Cys	
	10 15 20	
	tcg aaa acc cat agc ttg aaa ggc ctg gcc agg gga gga gca cag ata	450
	Ser Lys Thr His Ser Leu Lys Gly Leu Ala Arg Gly Gly Ala Gln Ile	
5	25 30 35 40	
	ttt tcc tgt ata att cca gaa tgt ctt cag aga gcc gtg cat gga ttg	498
	Phe Ser Cys Ile Ile Pro Glu Cys Leu Gln Arg Ala Val His Gly Leu	
	45 50 55	
	ctt cat tac ctt ttc cat acg aga aac cac acc ttc att gtc ctg cac	546
10	Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe Ile Val Leu His	
	60 65 70	
	ctg gtc ttg caa ggg atg gtt tat act gag tac acc tgg gaa gta ttt	594
	Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr Trp Glu Val Phe	
	75 80 85	
15	ggc tac tgt cag gag ctg gag ttg tcc ttg cat tac ctt ctt ctg ccc	642
	Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr Leu Leu Leu Pro	
	90 95 100	
	tat ctg ctg cta ggt gta aac ctg ttt ttt ttc acc ctg act tgt gga	690
	Tyr Leu Leu Leu Gly Val Asn Leu Phe Phe Phe Thr Leu Thr Cys Gly	
20	105 110 115 120	
	acc aat cct ggc att ata aca aaa gca aat gaa tta tta ttt ctt cat	738
	Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu Leu Phe Leu His	
	125 130 135	
	gtt tat gaa ttt gat gaa gtg atg ttt cca aag aac gtg agg tgc tct	786
25	Val Tyr Glu Phe Asp Glu Val Met Phe Pro Lys Asn Val Arg Cys Ser	
	140 145 150	
	act tgt gat tta agg aaa cca gct cga tcc aag cac tgc agt gtg tgt	834
	Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Lys His Cys Ser Val Cys	
	155 160 165	
30	aac tgg tgt gtg cac cgt ttc gac cat cac tgt gtt tgg gtg aac aac	882
	Asn Trp Cys Val His Arg Phe Asp His His Cys Val Trp Val Asn Asn	
	170 175 180	
	tgc atc ggg gcc tgg aac atc agg tac ttc ctc atc tac gtc ttg acc	930
	Cys Ile Gly Ala Trp Asn Ile Arg Tyr Phe Leu Ile Tyr Val Leu Thr	
35	185 190 195 200	

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978	ttg acg gcc tcg gct gcc acc gcc acc att gtc agc acc acc att ctg	205	210	215	1026	gtc cac ttg gtc gtc gtc tca gat tta tca cag gag act tca acc gat	220	225	230	1074	gac ctt gga cac ctc cat gtt atg gac acc gtc ttt ctt acc tac	235	240	245	1122	ctg ttc ctg acc ttt cca cgg att gtc ttc atg ctg ggc ttt gtc gtc	250	255	1170	ggt ctg acc ctg ctg ggc tac ctg ttg ctg ttg ctg ttg ctg	265	270	275	280	1218	gcg gcc acc aac cag act act aac gag ttg tac aga ggt gac ttg ggc	285	290	295	1266	ttg tgc cag gct tgt ccc ctt gtc gcc ttg cct ccg tca gca gag ccc	300	305	310	1314	caa gtc cac cgg aac att cac tcc cat ggg ctt cgg agc aac ctt caa	315	320	325	1362	gln val his arg asn ile his ser his gly leu arg ser asn leu gln	330	335	340	1420	tgacaagtgt atgacctgccct ttgagctgta gttcccgctt atttaacacat gtggatcc	1432	tcgtttcca ag	30	<210> 28	<211> 601	<212> DNA	<213> Homo sapiens	<220>	35
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&lt;221&gt; CDS

&lt;222&gt; (62)...(355)

&lt;400&gt; 28

5	atgcgcacat agcgacttgg tgggcgcgtc cagtgatgac tgggggatcc cggcaagtaa	60
	c atg act aaa aag aag cgg gag aat ctg ggc gtc gct cta gag atc gat	109
	Met Thr Lys Lys Lys Arg Glu Asn Leu Gly Val Ala Leu Glu Ile Asp	
	1                      5                      10                      15	
	ggg cta gag gag aag ctg tcc cag tgt cgg aga gac ctg gag gcc gtg	157
10	Gly Leu Glu Glu Lys Leu Ser Gln Cys Arg Arg Asp Leu Glu Ala Val	
	20                      25                      30	
	aac tcc aga ctc cac agc cgg gag ctg agc cca gag gcc agg agg tcc	205
	Asn Ser Arg Leu His Ser Arg Glu Leu Ser Pro Glu Ala Arg Arg Ser	
	35                      40                      45	
15	ctg gag aag gag aaa aac agc cta atg aac aaa gcc tcc aac tac gag	253
	Leu Glu Lys Glu Lys Asn Ser Leu Met Asn Lys Ala Ser Asn Tyr Glu	
	50                      55                      60	
	aag gaa ctg aag ttt ctt cgg caa gag aac cgg aag aac atg ctg ctc	301
	Lys Glu Leu Lys Phe Leu Arg Gln Glu Asn Arg Lys Asn Met Leu Leu	
20	65                      70                      75                      80	
	tct gtg gcc atc ttt atc ctc ctg acg ctc gtc tat gcc tac tgg acc	349
	Ser Val Ala Ile Phe Ile Leu Leu Thr Leu Val Tyr Ala Tyr Trp Thr	
	85                      90                      95	
	atg tgagcctggc acttccccac aaccagcaca ggcttccact tggcccct	400
25	Met	
	tgatcaggat caagcaggca cttcaagcct caataggacc aaggtgctgg ggtgttcccc	460
	tcccaacctg gtgttcaagc atggttccct ggcgcccag gccttgccct cctggcctgc	520
	tgggggggttc cgggtctcca gaaggacatg gtgctgggtcc ctcccttagc ccaagggaga	580
30	ggcaataaag acacaaagct g	601

&lt;210&gt; 29

&lt;211&gt; 585

&lt;212&gt; DNA

35 &lt;213&gt; Homo sapiens

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<220>  
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<222> (78)...(452)

5	<400> 29	actaacctct gccctgcagc cgcgagggcg cgcgggaat ccgagtgca tctgaaatac gcagagtcag taagacc atg gct acg tcc tcg atg tct aag ggt tgc ttt Met Ala Thr Ser Ser Met Ser Lys Gly Cys Phe	1	5	10
10		Val Phe Lys Pro Asn Ser Lys Lys Arg Lys Ile Ser Leu Pro Ile Glu gac tat ttt aac aaa ggg aaa aat gag cct gag gac agt aag ctt cga	15	20	25
15		Asp Tyr Phe Asn Lys Gly Lys Asn Glu Pro Glu Asp Ser Lys Leu Arg ttc gaa act tat cag ttg ata tgg cag cag atg aaa tct gaa aat gag	30	35	40
20		Arg Leu Glu Glu Glu Leu Asn Lys Asn Leu Phe Asp Asn Leu Ile Glu cga cta caa gag gaa tta aat aaa aac ttg ttt gac aat ctg att gaa	45	50	55
25		Phe Glu Thr Tyr Glu Leu Ile Trp Glu Glu Met Lys Ser Glu Asn Glu ggc ggt caa ata aaa ctc aga gaa att cca act gct gct att gct ctt	60	65	70
30		Gly Ile Tyr Ala Tyr Val Cys Ser Cys Met His Leu Cys Val Phe Arg ggt ata tat gcg tat gtt tgt tca tgc atg cat ctc tgt gta ttt cgt	75	80	85
35		Phe Leu Glu Lys Ser His Ser Gly Phe Glu Lys Asn Ser Arg Asp Leu ttt ctg caa aaa tca cat tct gga ttc cag aag aat tca aga gac ttg	90	95	100
40		Gly Gly Glu Ile Lys Leu Arg Glu Ile Pro Thr Ala Ala Leu Val Leu ggt ata tat gcg tat gtt tgt tca tgc atg cat ctc tgt gta ttt cgt	105	110	115
45		Gly Ile Tyr Ala Tyr Val Cys Ser Cys Met His Leu Cys Val Phe Arg ttt caaatcttt ttatctgtg agaatagtgg aaggaacctgt ttgatgagc c	120	125	130
50					
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 5 <213> Homo sapiens  
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 Met  
 1  
 gcc gag ctc ccg ggg ccc ttt ctc tgc ggg gcc ctg cta ggc ttc ctg 107  
 15 Ala Glu Leu Pro Gly Pro Phe Leu Cys Gly Ala Leu Leu Gly Phe Leu  
 5 10 15  
 tgc ctg agt ggg ctg gcc gtg gag gtg aag gta ccc aca gag ccg ctg 155  
 Cys Leu Ser Gly Leu Ala Val Glu Val Lys Val Pro Thr Glu Pro Leu  
 20 25 30  
 20 agc acg ccc ctg ggg aag aca gcc gag ctg acc tgc acc tac agc acg 203  
 Ser Thr Pro Leu Gly Lys Thr Ala Glu Leu Thr Cys Thr Tyr Ser Thr  
 35 40 45  
 tcg gtg gga gac agc ttc gcc ctg gag tgg agc ttt gtg cag cct ggg 251  
 Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser Phe Val Gln Pro Gly  
 25 50 55 60 65  
 aaa ccc atc tct gag tcc cat cca atc ctg tac ttc acc aat ggc cat 299  
 Lys Pro Ile Ser Glu Ser His Pro Ile Leu Tyr Phe Thr Asn Gly His  
 70 75 80  
 ctg tat cca act ggt tot aag tca aag cgg gtc agc ctg ctt cag aac 347  
 30 Leu Tyr Pro Thr Gly Ser Lys Ser Lys Arg Val Ser Leu Leu Gln Asn  
 85 90 95  
 ccc ccc aca gtg ggg gtg gcc aca ctg aaa ctg act gac gtc cac ccc 395  
 Pro Pro Thr Val Gly Val Ala Thr Leu Lys Leu Thr Asp Val His Pro  
 100 105 110  
 35 tca gat act gga acc tac ctc tgc caa gtc aac aac cca cca gat ttc 443

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5	115	Ser Asp Thr Gly Thr Tyr Leu Cys Gln Val Asn Asn Pro Pro Asp Phe	120	125	491
	130	Tyr Thr Asn Gly Leu Ile Asn Leu Thr Val Leu Val Pro Pro	135	140	145
10	165	Thr Ala Leu Arg Cys Ser Ser Ser Ser Ser Ser Ser Ser Ser	170	175	587
	180	Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser Met	185	190	635
15	195	Val Gln Asp Gln Val Ser Gly Gln Leu Ile Leu Thr Asn Leu Ser Leu	200	205	683
	210	gac tcc tcc ggc acc tac cgc tgc ggc acc aac cag atg ggc agt	215	220	731
20	225	Thr Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly Ser	230	235	779
	245	Ala Ser Cys Gln Leu Thr Leu Ser Val Thr Gln Pro Ser Gln Gly Arg	250	255	827
25	260	Val Ala Gly Ala Leu Ile Gly Val Leu Leu Gly Val Leu Leu Ser	265	270	875
	275	gac tcc tcc ggc acc tac cgc tgc ggc acc aac cag atg ggc agc	280	285	923
30	290	Pro Lys Gln Thr Tyr Gly Gly Ser Asp Leu Arg Gln Asp Ala Ile Ala	295	300	971
	305	cct ggc atc tct gag cac act tgc atg agc gct gat tct agc aag ggc			
35	310	Pro Gly Ile Ser Gln His Thr Cys Met Arg Ala Asp Ser Ser Lys Gly	315	320	
	320	cct ggc atc tct gag cac act tgc atg agc gct gat tct agc aag ggc	325	330	



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ttc ctg gaa aga ccc tcg tct gcc agc acc gtg acg acc acc aag tcc 1019  
 Phe Leu Glu Arg Pro Ser Ser Ala Ser Thr Val Thr Thr Thr Lys Ser  
 310 315 320  
 aag ctc cct atg gtc gtg tgacttctcc cgatccctga gggcgggtgag ggg 1070  
 5 Lys Leu Pro Met Val Val  
 325  
 gaatatcaat aattaaagtc tgtgggtacc 1100  
  
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 10 <211> 313  
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 1 5 10 15  
 Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser  
 20 25 30  
 Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys  
 20 35 40 45  
 Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val  
 50 55 60  
 Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr  
 65 70 75 80  
 25 Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val  
 85 90 95  
 Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu  
 100 105 110  
 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala  
 30 115 120 125  
 Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala  
 130 135 140  
 Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His  
 145 150 155 160  
 35 Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu

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35	Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu	50	55	60
	Tyr Glu Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Glu Val	35	40	45
30	Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Glu Lys Glu Cys Phe	20	25	30
	Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu	5	10	15
	Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala			
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	<212> PRT			
	<211> 229			
20	<210> 32			
	305			
	Glu Ala Ala Val Leu Leu Phe Tyr Arg	310		
	290			
	Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr	295		
15	275			
	Pro Glu Ala Ser Pro Glu Glu Cys Gly Asp Phe Ser Gly Phe Asp Trp	280		
	260			
	Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe	265		
	245			
	Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val	250		
10	225			
	Pro Tyr Gly Glu Arg Glu Phe Thr Ala Gly Phe Val Glu Phe Arg Val	230		
	210			
	Val Val Tyr Asp Phe Gly Asp Ala Glu Lys Thr Ala Ser Tyr Tyr Ser	215		
5	195			
	Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro	200		
	180			
	Glu Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Glu Lys Tyr Pro Val	185		
	165			
	170			
	175			

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65                      70                      75                      80  
 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr  
                          85                      90                      95  
 Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe  
 5                      100                      105                      110  
 Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn  
                          115                      120                      125  
 Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr  
                          130                      135                      140  
 10 Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile  
                          145                      150                      155                      160  
 Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu  
                          165                      170                      175  
 Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe  
 15                      180                      185                      190  
 Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val  
                          195                      200                      205  
 Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys  
                          210                      215                      220  
 20 Arg Lys Ser Arg Thr  
                          225  
  
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 25 <212> PRT  
      <213> Homo sapiens  
  
 <400> 33  
 Met Arg Pro Gln Glu Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu  
 30       1                      5                      10                      15  
 Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr  
                          20                      25                      30  
 Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala  
                          35                      40                      45  
 35 Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe

	5	10	15	20	25	30	35
Ser Val Pro Ser Phe Gly Ser Gln Trp Phe Trp Tyr Trp Gln Lys	65	70	75	80			
Gln Lys Ile Pro Lys Tyr Val Gln Phe Met Lys Asp Asn Tyr Pro Pro	85	90	95				
Ser Phe Lys Tyr Gln Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe	100	105	110				
Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr	115	120	125				
Ile Val Leu Thr Ser Lys His His Gln Gly Phe Thr Leu Trp Gly Ser	130	135	140				
Gln Tyr Ser Trp Asn Trp Asn Ala Ile Asp Gln Gly Pro Lys Arg Asp	145	150	155	160			
Ile Val Lys Gln Leu Gln Val Ala Ile Arg Asn Arg Thr Asp Leu Arg	165	170	175				
Phe Gly Leu Tyr Tyr Ser Leu Phe Gln Trp Phe His Pro Leu Phe Leu	180	185	190				
Gln Asp Gln Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys	195	200	205				
Thr Leu Pro Gln Leu Tyr Gln Leu Val Asn Asn Tyr Gln Pro Gln Val	210	215	220				
Leu Trp Ser Asp Gly Asp Gly Ala Pro Asp Gln Tyr Trp Asn Ser	225	230	235	240			
Thr Gly Phe Leu Ala Trp Leu Tyr Asn Gln Ser Pro Val Arg Gly Thr	245	250	255				
Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly	260	265	270				
Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro	275	280	285				
His Lys Trp Gln Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr	290	295	300				
Arg Arg Gln Ala Gly Ile Ser Asp Tyr Leu Thr Ile Gln Leu Val	305	310	315	320			
Lys Gln Leu Val Gln Thr Val Ser Cys Gly Asn Leu Met Asn	325	330	335				

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Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg  
                   340                                  345                                  350  
 Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr  
                   355                                  360                                  365  
 5 Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val  
                   370                                  375                                  380  
 Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu  
                   385                                  390                                  395                                  400  
 Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile  
 10                                   405                                  410                                  415  
 Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn  
                   420                                  425                                  430  
 Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu  
                   435                                  440                                  445  
 15 Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr  
                   450                                  455                                  460  
 Asn Val Ile  
                   465  
  
 20 <210> 34  
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     <212> PRT  
     <213> Homo sapiens  
  
 25 <400> 34  
 Met Asp Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser  
       1                                  5                                  10                                  15  
 Val Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu  
                   20                                  25                                  30  
 30 Val Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro  
                   35                                  40                                  45  
 Glu Thr Thr Thr Leu Thr Val Gly Gly Gly Val Phe Ala Leu Val Thr  
                   50                                  55                                  60  
 Ala Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu  
 35                   65                                  70                                  75                                  80

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phe Asn pro Ser Gly pro Tyr Gln Gln Lys pro Val His Gln Lys Lys  
85 90 95  
Gln Val Leu

5

<210> 35

<211> 189

<212> PRT

<213> Homo sapiens

10

<400> 35

Met Gln Gln Gly Gly Asn Leu Gly Gly Ile Lys Met Val His Leu  
1 5 10 15

Leu Val Leu Ser Gly Ala Trp Gly Met Gln Met Trp Val Thr Phe Val  
20 25 30

15

Ser Gly Phe Leu Leu Phe Arg Ser Leu Pro Arg His Thr Phe Gly Leu  
35 40 45

Val Gln Ser Lys Leu Phe Pro Phe Tyr Phe His Ile Ser Met Gly Cys  
50 55 60

Ala Phe Ile Asn Leu Cys Ile Leu Ala Ser Gln His Ala Trp Ala Gln  
65 70 75 80

20

Leu Thr Phe Trp Gln Ala Ser Gln Leu Tyr Leu Leu Phe Leu Ser Leu  
85 90 95

Thr Leu Ala Thr Val Asn Ala Arg Trp Leu Gln Pro Arg Thr Thr Ala  
100 105 110

Ala Met Trp Ala Leu Gln Thr Val Gln Lys Gln Arg Gly Leu Gly Gly  
115 120 125

25

Gln Val Pro Gly Ser His Gln Gly Pro Asp Pro Tyr Arg Gln Leu Arg  
130 135 140

Gln Lys Asp Pro Lys Tyr Ser Ala Leu Arg Gln Asn Phe Phe Arg Tyr  
145 150 155 160

30

His Gly Leu Ser Ser Leu Cys Asn Leu Gly Cys Val Leu Ser Asn Gly  
165 170 175

35

Leu Cys Leu Ala Gly Leu Ala Leu Gln Ile Arg Ser Leu  
180 185

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&lt;210&gt; 36

&lt;211&gt; 363

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

5

&lt;400&gt; 36

Met Val Asp Ser Leu Leu Ala Val Thr Leu Ala Gly Asn Leu Gly Leu  
 1 5 10 15  
 Thr Phe Leu Arg Gly Ser Gln Thr Gln Ser His Pro Asp Leu Gly Thr  
 10 20 25 30  
 Glu Gly Cys Trp Asp Gln Leu Ser Ala Pro Arg Thr Phe Thr Leu Leu  
 35 40 45  
 Asp Pro Lys Ala Ser Leu Leu Thr Lys Ala Phe Leu Asn Gly Ala Leu  
 50 55 60  
 15 Asp Gly Val Ile Leu Gly Asp Tyr Leu Ser Arg Thr Pro Glu Pro Arg  
 65 70 75 80  
 Pro Ser Leu Ser His Leu Leu Ser Gln Tyr Tyr Gly Ala Gly Val Ala  
 85 90 95  
 Arg Asp Pro Gly Phe Arg Ser Asn Phe Arg Arg Gln Asn Gly Ala Ala  
 100 105 110  
 20 Leu Thr Ser Ala Ser Ile Leu Ala Gln Gln Val Trp Gly Thr Leu Val  
 115 120 125  
 Leu Leu Gln Arg Leu Glu Pro Val His Leu Gln Leu Gln Cys Met Ser  
 130 135 140  
 25 Gln Glu Gln Leu Ala Gln Val Ala Ala Asn Ala Thr Lys Glu Phe Thr  
 145 150 155 160  
 Glu Ala Phe Leu Gly Cys Pro Ala Ile His Pro Arg Cys Arg Trp Gly  
 165 170 175  
 Ala Ala Pro Tyr Arg Gly Arg Pro Lys Leu Leu Gln Leu Pro Leu Gly  
 180 185 190  
 30 Phe Leu Tyr Val His His Thr Tyr Val Pro Ala Pro Pro Cys Thr Asp  
 195 200 205  
 Phe Thr Arg Cys Ala Ala Asn Met Arg Ser Met Gln Arg Tyr His Gln  
 210 215 220  
 35 Asp Thr Gln Gly Trp Gly Asp Ile Gly Tyr Ser Phe Val Val Gly Ser

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225	230	235	240
Asp Gly Tyr Val Tyr Gly Arg Gly Trp His Trp Val Gly Ala His			
245	250	255	
Thr Leu Gly His Asn Ser Arg Gly Phe Gly Val Ala Ile Val Gly Asn			
260	265	270	
Tyr Thr Ala Ala Leu Pro Thr Glu Ala Ala Leu Arg Thr Val Arg Asp			
275	280	285	
Thr Leu Pro Ser Cys Ala Val Arg Ala Gly Leu Leu Arg Pro Asp Tyr			
290	295	300	
Ala Leu Leu Gly His Arg Glu Leu Val Arg Thr Asp Cys Pro Gly Asp			
305	310	315	320
Ala Leu Phe Asp Leu Leu Arg Thr Trp Pro His Phe Thr Ala Thr Val			
325	330	335	
Lys Pro Arg Pro Ala Arg Ser Val Ser Lys Arg Ser Arg Arg Glu Pro			
340	345	350	
Pro Pro Arg Thr Leu Pro Ala Thr Asp Leu Glu			
355	360		
<210> 37			
<211> 249			
<212> PRT			
<213> Homo sapiens			
25	1	5	10
Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala Gly Leu Leu Leu			
1	5	10	15
Gly Ala Gly Ala Cys Tyr Cys Ile Tyr Arg Leu Thr Arg Gly Arg Arg			
20	25	30	
Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys Ser Ala Glu Asp			
35	40	45	
Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala Glu Glu Leu Glu			
50	55	60	
Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro Val Ile Ile Glu			
65	70	75	80
Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Ala Phe Ser Val Asn Glu			
35			



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	85	90	95
	Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val Ala Asn Lys Ile		
	100	105	110
5	Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu Asn Ala Leu Asn		
	115	120	125
	Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile Lys Val Gln Val		
	130	135	140
	Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala Met Thr Glu Gly		
	145	150	155
10	Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser Leu Tyr Asp Ser		
	165	170	175
	His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr Leu Phe Gln Asn		
	180	185	190
	Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala Val Gln Pro Thr		
15	195	200	205
	Phe Thr Glu Gly Ser Leu Phe Phe Leu Leu His Gly Glu Glu Cys Ala		
	210	215	220
	Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala Glu Val Lys Glu		
	225	230	235
20	Lys Val Val Thr Ile Ile Pro Lys Ile		
	245		
	<210> 38		
	<211> 98		
25	<212> PRT		
	<213> Homo sapiens		
	<400> 38		
	Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile		
30	1	5	10
	Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe		
	20	25	30
	Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu		
	35	40	45
35	Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln		

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50 55 60  
Val Ser Tyr Asn Cys Phe Ile Ala Gly Leu Tyr Leu Leu Gly  
65 70 75 80  
Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Gln Tyr Met  
85 90 95  
Val Arg

<210> 39

<211> 172

<212> PRT

<213> Homo sapiens

10

Met Val Gly Pro Ala Pro Arg Arg Arg Leu Arg Pro Leu Ala Ala Leu  
1 5 10 15  
Ala Leu Val Leu Ala Leu Ala Pro Gly Leu Pro Thr Ala Arg Ala Gly  
20 25 30  
Gln Thr Pro Arg Pro Ala Gln Arg Gly Pro Pro Val Arg Leu Phe Thr  
35 40 45  
Gln Gln Gln Leu Ala Arg Tyr Gly Gly Gln Gln Asp Gln Pro Ile  
50 55 60  
Tyr Leu Ala Val Lys Gly Val Phe Asp Val Thr Ser Gly Lys Gln  
65 70 75 80  
Phe Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Thr Gly Lys Asp Ser  
85 90 95  
Thr Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His  
100 105 110  
Asp Thr Gly Leu Thr Ala Lys Gln Leu Gln Ala Leu Asp Gln Val  
115 120 125  
Phe Thr Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala  
130 135 140  
Arg Arg Ile Leu Asn Gln Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro  
145 150 155 160  
Gln Asp Gln Pro His Phe Asp Ile Lys Asp Gln Phe  
165 170

15

20

25

30

35

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<210> 40  
 <211> 120  
 <212> PRT  
 5 <213> Homo sapiens

<400> 40  
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 1 5 10 15  
 10 Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile Asp Leu  
 20 25 30  
 Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile Ala Leu  
 35 40 45  
 Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile Gly Ser  
 15 50 55 60  
 Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg Ala Val  
 65 70 75 80  
 Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe Tyr His  
 85 90 95  
 20 Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr Ser Tyr  
 100 105 110  
 Asp Asp Ile Pro Asp Phe Asp Asp  
 115 120

25 <210> 41  
 <211> 939  
 <212> DNA  
 <213> Homo sapiens

30 <400> 41  
 atgaaccaac toagcttctc gctgtttctc atagcgacca ccagaggatg gagtacagat 60  
 gaggctaata ettacttcaa ggaatggacc tgttctctct ctecatctct gccagaagc 120  
 tgcaaggaaa tcaaagacga atgtcctagt gcatttgatg gcctgtattt tctccgcact 180  
 gagaatggtg ttatctacca gaccttctgt gacatgacct ctgggggtgg cgctgggacc 240  
 35 ctggtggcca gcgtgcatga gaatgacatg cgtgggaagt gcacggtggg cgatcgctgg 300

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35	<210> 43 <211> 1401 <212> DNA <213> Homo sapiens	
30	tttggagata agagagaaag tagaac gttaatttag tgggtcatggt ggtgggtgca gccattcgaag ttatatgct gaagagtcg	687 660 600 540 480 420 360 300 240 180 120 60
25	ttctttgaaat taatccctggaa taatatggga gaacagggcaac aagaaacaaag aagattggaa gttgggtgatt acaatgctcg ctttgacaaat acaatcgaag caattcctga gaaggtgatt	
20	atgggcgaac agatcctggt gccctccac gtcctccctc tggccgctc gccctccggt cccgccggcc agaaaggagtg cttccacaa gccctccac cttccacaa gccctccac cttccacaa	
15	<210> 42 <211> 687 <212> DNA <213> Homo sapiens	
10	cgtagagataa ctgaagcaga tgtgcttcta ttctatcgt ggagattttt ctggttttga ttggagtgga tatggaaacc atgttggtta cagcagcaga	939 900 840 780 720 660 600 540 480 420 360
5	ttcagtcagc aggcagactac cagagagggg aagcgaactg ggcgaactac aaacaccttg gatctgcaaga ggcggccacg agcgatgaaat acaagaaacc tggctactac gaactcgaag caagagacct ggcactcgg caagctgcac ataaatccac catgcagacac catabatcgt ttggcaatca caagaaatat caagtgaat atggagagag aagtgctg actgaacaaag gcccggtgat cctgtggtc tatgatcttg ggcagcgccaa gaacacagca tcttatctac cacctatgg ccagcgggga ttcaatgcgg gatctgtcca gttcaagggtta tttatataag agagagcaga caacggcctg tgtgctggaa tgaaggctcac cggatctaac actgaagcac actgcattgg tgaaggaaga taattccaa aggcaggtcc cagcagtggt ggagattttt ctggttttga ttggagtgga tatggaaacc atgttggtta cagcagcaga	

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<400> 43	
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	ctgcgcgcgc cgccgtgccc tgcccacagc gccacgcgct tegacccac ctgggagtc 120
5	ctggacgccc gccagctgcc cgcgtggttt gaccaggcca agttcggcat cttcatccac 180
	tggggagtgt tttccgtgcc cagcttcggg agcagtggt tctggtggtt ttggcaaaag 240
	gaaaagatac cgaagtatgt ggaatttatg aaagataatt accctcctag tttcaaatat 300
	gaagattttg gaccactatt tacagcaaaa ttttttaatg ccaaccagtg ggcagatatt 360
	tttcaggcct ctggtgcaa atacattgtc ttaacttcca aacatcatga aggctttacc 420
10	ttgtgggggt cagaatatcc gtggaactgg aatgccatag atgaggggcc caagaggggac 480
	attgtcaagg aacttgaggt agccattagg aacagaactg acctgcgttt tggactgtac 540
	tattcccttt ttgaatggtt tcatccgctc ttccttgagg atgaatccag ttcattccat 600
	aagcggaat ttccagtttc taagacattg ccagagctct atgagttagt gaacaactat 660
	cagcctgagg ttctgtggtc ggatggtgac ggaggagcac cggatcaata ctggaacagc 720
15	acaggcttct tggcctgggt atataatgaa agcccagttc ggggcacagt agtcaccaat 780
	gacgtgtggg gagctggtag catctgtaag catggtggct tctataacctg cagtgatcgt 840
	tataaccag gacatctttt gccacataaa tgggaaaact gcatgacaat agacaaaactg 900
	tcctggggct ataggaggga agctggaatc tctgactatc ttacaattga agaattggtg 960
	aagcaacttg tagagacagt ttcattgtgga ggaaatcttt tgatgaatat tggggccaca 1020
20	ctagatggca ccattttctgt agtttttgag gagcgactga ggcaaatggg gtccctggcta 1080
	aaagtcaatg gagaagctat ttatgaaacc catacctggc gatcccagaa tgacactgtc 1140
	accccagatg tgtggtacac atccaagcct aaagaaaaat tagtctatgc cttttttctt 1200
	aatggccca catcaggaca gctgttcctt ggccatccca aagctattct gggggcaaca 1260
	gaggtgaaac tactgggcca tggacagcca cttaactgga tttctttgga gcaaatggc 1320
25	attatggtag aactgccaca gctaaccatt catcagatgc cgtgtaaatg gggctgggct 1380
	ctagccctga ctaatgtgat c 1401
<210> 44	
<211> 297	
30	<212> DNA
<213> Homo sapiens	
<400> 44	
	atggataacg tgcagcgaa aataaaacat cgcccttct gcttcagtgt gaaaggccac 60
35	gtgaagatgc tgcggctgga tattatcaac tcaactggtaa caacagtatt catgtcatc 120

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gtatctgtgt tggacatgat accagaaac acatcatga cagtgtgtgg aggtgtgttt 180  
gacatgttga cagcagtatg ctgtcttgcc gacgggtggcc ttatttacgg gaagcttcg 240  
ttcaatccca gctgtctcta ccagcaaaag cctgtgtcatg aaaaaaaga agtttg 297

5

<210> 45

<211> 567

<212> DNA

<213> Homo sapiens

10

<400> 45

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gttgcctggg gcattgcataat gttggttgacc ttccgtctcag gcttcctgct ttccggaaag 120  
cttcccccgaac ataccctcgg actaagtccag agcaaaacct tccccttcta cttccacaatc 180  
tcaatgtgct gtgccttcat caacctcgcg atcttggtct caacagcatgc ttgggtctcag 240  
ctcaacatct gggagggccag ccagcttcta cgtctgttcc tgaagcttae gcttggccact 300  
gtcaaacgcc gccgtgtcga acccccgaac acagcttcca tgttgggtccct gcaaaacctg 360  
gagaaaggagc gaggcctggg ttgggttggtta ccaggtggtcc cgtaccctta 420  
cgcaagcttc gaggaggaag ccccaagtac agtgcctccc gccaggaatt cttccgttca 480  
catgggtgtt cctctcttg caatctgggg tgcgtctcga gcaatgggtt ctgtctcgtt 540  
ggccttggcc tggaaataag gaggctc 567

30

atgtgttgaca gctcctcctggc agtcaacctg gcttgaaacc ttgggtctga cttcctccga 60  
gtttcccaaga cccagagcca tccaggaacctg ggaacctgagg gctgtctggga ccagctctct 120  
ggccctcggga cctttacgct ttctggaccac aaggcatctc tgttaacaa ggccctctcc 180  
aatgggcgcc ttggatgggtt catctcttga gacataacct gaccgtacatc tgaagccccc 240  
ccatccctca gccacttgcct gaggccagtac tatgggggtcgg ggttggccag agaacccagg 300  
ttccgcagca acctcccgacc gcaagaaacct gctgtctcga cttcagacct catccctggc 360  
cagcaggtgt ggggaacctt tgtccttcta caggaggtcgg agccagttaca cctccagctt 420  
cagttcatga gcccaagaca gctggccca atgtctacca ggaattcaact 480

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gaggccttcc tgggatgcc gccatccac ccccgctgcc gctggggagc ggcgccttat 540  
 cggggcgcc cgaagctgct gcagctgccg ctgggattct tgtacgtgca tcacacctac 600  
 gtgcctgcac caccctgcac ggacttcacg cgctgcgcag ccaacatgcg ctccatgcag 660  
 cgtaccacc aggacacgca aggetgggga gacatcggt acagtctcgt ggtgggctcg 720  
 5 gacggctacg tgtacgagg acgcggtcg cactgggtgg gcgcccacac gctcggccac 780  
 aactcccggt gettcggcgt ggccatagt ggcaactaca ccgcgcgct gccaccgag 840  
 gccgctctgc gcacggtgcg cgacacgctc ccgagttgtg cgggtgcgcg cggcctcctg 900  
 cggccagact acgcgctgct gggccaccgc cagctggtgc gcaccgactg ccccgcgac 960  
 gcgctcttcg acctgctgcg cactggccg cacttcaccg cgactgttaa gccaagacct 1020  
 10 gccaggagt tctctaagag atccaggagg gagccacccc caaggacct gccagccaca 1080  
 gacctccaa 1089

&lt;210&gt; 47

&lt;211&gt; 747

15 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

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 20 tctactgca ttacaggct gaccggggt cgcgggcgga gcgaccgga gctcgggata 120  
 cgctcttcga agtccgcaga agacttaact gatggttcat atgatgatgt tctaatgct 180  
 gaacaacttc agaaactcct ttacctgctg gagtcaacgg aggatcctgt aattattgaa 240  
 agagctttga ttactttggg taacaatgca gccttttcag ttaaccaagc tattattcgt 300  
 gaattgggtg gtattccaat tgttgcaaac aaaatcaacc attccaacca gagtattaaa 360  
 25 gagaaagctt taaatgcact aaataacctg agtgtgaatg ttgaaaatca aatcaagata 420  
 aagggtgcaag ttttgaaact gcttttgaat ttgtctgaaa atccagccat gacagaagga 480  
 cttctccgtg cccaagtga ttcatcattc cttcccttt atgacagcca cgtagcaag 540  
 gagattcttc ttcgagtact tacgtatatt cagaatataa agaactgcct caaaatagaa 600  
 ggccatttag ctgtgcagcc tactttcact gaagggtcat tgtttttcct gttacatgga 660  
 30 gaagaatgtg ccagaaaat aagagcttta gttgatcacc atgatgcaga ggtgaaggaa 720  
 aagggtgtaa caataatacc caaaatc 747

&lt;210&gt; 48

&lt;211&gt; 294

35 &lt;212&gt; DNA

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<213> Homo sapiens

<400> 48

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tggggagtcga tcatgttcgat aatgtctcgga atatctttca atgtccatcc cgtgtgttg  
atcgaggagc tcccttcac gggagaaagat ttctggagatg gcccccagaa catatcacac  
cttcagagac aagtcagctc caactgttc atcgcctgcag gctcttcact cctcctcgga  
ggcttctctt tctgcacagt tctgcctcaat aagccgaaag aatacatgtg gccg  
294

10

<210> 49

<211> 516

<212> DNA

<213> Homo sapiens

15

<400> 49

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gatacagccca tctaccttggc agtggaaaggga gtcgtgttctg atgtccaccc cggaaaggag  
tttataggac gaggagcccc ctacaatatgc ttgacggggga aggacctccac tgaagggtgtta  
ggcaagatgt ccttggatcc tgcagagacc acccatggaca ctacgggtct caggcccaag  
gaaactggagc ccttggatga ggtcttcacc aaagtgttaca aagccaaata ccccatcgtc  
ggctacacctg ccgggagaaat tctcaatgag gatggcgagcc ctacacctgga cttcaagct  
gaaagacacgc cccatcttga catcaaggat gagttc  
516

25

<210> 50

<211> 360

<212> DNA

<213> Homo sapiens

30

<400> 50

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atccctata aggcacatccg acttgcact gtcgtgttct tgaattggcg cttctcact  
atataggtc cctcctcgt gtcaggtac atcaggtac atcagcaaaag ggggggcaga ccgggcctt  
240

35



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ccagtgetga tcattggcat tctgggtgttc ctaccoggat tttaccacct ggcatoget 300  
tactatgcat ccaaaggcta cegtgggttac tcctatgatg acattocaga ctttgatgac 360

<210> 51  
5 <211> 1065  
<212> DNA  
<213> Homo sapiens  
<220>  
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10 <222> (2)...(943)

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15 1 5 10 15  
tgg agt aca gat gag gct aat act tac ttc aag gaa tgg acc tgt tct 97  
Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser  
20 20 25 30  
tcg tct cca tct ctg ccc aga agc tgc aag gaa atc aaa gac gaa tgt 145  
Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys  
35 40 45  
cct agt gca ttt gat ggc ctg tat ttt ctc cgc act gag aat ggt gtt 193  
Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val  
50 55 60  
25 atc tac cag acc ttc tgt gac atg acc tct ggg ggt ggc ggc tgg acc 241  
Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr  
65 70 75 80  
ctg gtg gcc agc gtg cat gag aat gac atg cgt ggg aag tgc acg gtg 289  
Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val  
30 85 90 95  
ggc gat cgc tgg tcc agt cag cag ggc agc aaa gca gac tac cca gag 337  
Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu  
100 105 110  
ggg gac ggc aac tgg gcc aac tac aac acc ttt gga tct gca gag gcg 385  
35 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala

433	gac acy agc gat gac tac aag aac cct ggc tac tac gac atc cag ggc	115	120	125
481	ala thr ser asp tyr lys asn pro gly tyr tyr asp ile gln ala	130	135	140
529	mag gac ctg ggc atc tgg cac gtg ccc aat aag tcc ccc atg cag cac	145	150	155
577	lys asp leu gly ile trp his val pro asn lys ser pro met gln his	160	165	170
625	ctg aga aac agc tcc ctg ctg agy agy tac cgc acg gac act ggc ttc ctc	175	180	185
673	trp arg asn ser ser leu leu arg tyr arg thr asp thr gly phe leu	190	195	200
721	cag aca ctg gga cat aat ctg ttt ggc atc tac cag aaa tac cca gty	205	210	215
769	gln thr leu gly his asn leu phe gly ile tyr gln lys tyr pro val	220	225	230
817	aaa tat gga gaa aag tgt tgg act gac aac ggc ccc gty atc cct	235	240	245
865	lys tyr gly gln gly lys cys trp thr asp asn gly pro val ile pro	250	255	260
913	aaa tat gga aac agc ttt ggc gac ggc cag aaa gca tct tat tac tca	265	270	275
960	val val tyr asp phe gly ala gln lys thr ala ser tyr tyr ser	280	285	290
		295	300	
				gag gca gct gtc ctt cta ttc cgt tgaagatttt gtgggagggga

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Glu Ala Ala Val Leu Leu Phe Tyr Arg  
 305 310  
 acccagacct ctctcccaa ccatgagatc ccaaggatgg agaacaactt acccagtagc 1020  
 tagaatgtta atggcagaag agaaaacaat aatcatatt gactc 1065

5  
 <210> 52  
 <211> 937  
 <212> DNA  
 <213> Homo sapiens

10  
 <220>  
 <221> CDS  
 <222> (177)...(866)

<400> 52

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 ggagcggaga caacagtacc tgacgcctct ttcagcccgg gatcgcccca gcaggg 176  
 atg ggc gac aag atc tgg ctg ccc ttc ccc gtg ctc ctt ctg gcc get 224  
 Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala

20 1 5 10 15  
 ctg cct ccg gtg ctg ctg cct ggg gcg gcc ggc ttc aca cct tcc ctc 272  
 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu  
 20 25 30  
 gat agc gac ttc acc ttt acc ctt ccc gcc ggc cag aag gag tgc ttc 320  
 25 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe  
 35 40 45  
 tac cag ccc atg ccc ctg aag gcc tcg ctg gag atc gag tac caa gtt 368  
 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val  
 50 55 60  
 30 tta gat gga gca gga tta gat att gat ttc cat ctt gcc tct cca gaa 416  
 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu  
 65 70 75 80  
 ggc aaa acc tta gtt ttt gaa caa aga aaa tca gat gga gtt cac act 464  
 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr

35 85 90 95

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512	gta gag act gaa gtt ggt gat tac atg ttc tgc ttt gac aat aca ttc	100	105	110	
	Val Gln Thr Gln Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe				
560	agc acc att tct gag aag gtg att ttc tta tta atc ctg gat aat	115	120	125	
	Ser Thr Ile Ser Gln Lys Val Ile Phe Phe Gln Leu Ile Leu Asp Asn				
608	atg gga gaa cag gca gaa gaa gat tgg aag aaa tat att act	130	135	140	
	Met Gly Gln Gln Ala Gln Gln Gln Asp Trp Lys Lys Tyr Ile Thr				
656	ggc aca gat ata tgg gat atg aaa ctg gaa gac atc ctg gaa tcc atc	145	150	155	160
	Gly Thr Asp Ile Leu Asp Met Lys Leu Gln Asp Ile Leu Gln Ser Ile				
704	aac agc atc aag tcc aya cta agc aaa agt ggg cac ata caa att ctg	165	170	175	
	Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu				
752	ctt aga gca ttt gaa gct cgt gat cga aac ata caa gaa agc aac ttt	180	185	190	
	Ileu Arg Ala Phe Gln Ala Arg Asp Arg Asn Ile Gln Gln Ser Asn Phe				
800	gat aga gtc aat ttc tgg tct atg gtc aat tta gtc atc atg gtc gtc	195	200	205	
	Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val				
848	gtg tca gcc att caa gtt tat atg ctg aag agt ctg ttt gaa gat aag	210	215	220	
	Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Gln Asp Lys				
900	agg aaa agt aya act taatactcca aactagagta cgttaacattg aaaaatg				
	Arg Lys Ser Arg Thr				
937	agggcatataaa atgcataaaa ctggtacagtc caagagcc				
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	<211> 1678				
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	<213> Homo sapiens				
	<220>				
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&lt;222&gt; (56)...(1459)

&lt;400&gt; 53

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5	atg cgg ccc cag gag ctc ccc agg ctc gcg ttc ccg ttg ctg ctg ttg	103
	Met Arg Pro Gln Glu Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu	
	1 5 10 15	
	ctg ttg ctg ctg ctg ccg ccg ccg ccg tgc cct gcc cac agc gcc acg	151
	Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr	
10	20 25 30	
	cgc ttc gac ccc acc tgg gag tcc ctg gac gcc cgc cag ctg ccc gcg	199
	Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala	
	35 40 45	
	tgg ttt gac cag gcc aag ttc ggc atc ttc atc cac tgg gga gtg ttt	247
15	Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe	
	50 55 60	
	tcc gtg ccc agc ttc ggt agc gag tgg ttc tgg tgg tat tgg caa aag	295
	Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys	
	65 70 75 80	
20	gaa aag ata ccg aag tat gtg gaa ttt atg aaa gat aat tac cct cct	343
	Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro	
	85 90 95	
	agt ttc aaa tat gaa gat ttt gga cca cta ttt aca gca aaa ttt ttt	391
	Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe	
25	100 105 110	
	aat gcc aac cag tgg gca gat att ttt cag gcc tct ggt gcc aaa tac	439
	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr	
	115 120 125	
	att gtc tta act tcc aaa cat cat gaa ggc ttt acc ttg tgg ggg tca	487
30	Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser	
	130 135 140	
	gaa tat tcg tgg aac tgg aat gcc ata gat gag ggg ccc aag agg gac	535
	Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp	
	145 150 155 160	
35	att gtc aag gaa ctt gag gta gcc att agg aac aga act gac ctg cgt	583

\_\_\_\_\_

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	ctg agg caa atg ggg tcc tgg cta aaa gtc aat gga gaa gct att tat	1159
	Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr	
	355 360 365	
	gaa acc cat acc tgg cga tcc cag aat gac act gtc acc cca gat gtg	1207
5	Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val	
	370 375 380	
	tgg tac aca tcc aag cct aaa gaa aaa tta gtc tat gcc att ttt ctt	1255
	Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu	
	385 390 395 400	
10	aaa tgg ccc aca tca gga cag ctg ttc ctt ggc cat ccc aaa gct att	1303
	Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile	
	405 410 415	
	ctg ggg gca aca gag gtg aaa cta ctg ggc cat gga cag cca ctt aac	1351
	Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn	
15	420 425 430	
	tgg att tct ttg gag caa aat ggc att atg gta gaa ctg cca cag cta	1399
	Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu	
	435 440 445	
	acc att cat cag atg ccg tgt aaa tgg ggc tgg gct cta gcc ctg act	1447
20	Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr	
	450 455 460	
	aat gtg atc taaagtgcag cagagtggct gatgctgcaa gttatgtcta aggc	1500
	Asn Val Ile	
	465	
25	taggaactat caggtgtcta taattgtagc acatggagaa agcaaatgta aaactggata	1560
	agaaaattat ttggcagtt cagcccttcc ccttttcc actaaatttt ttcttaaatt	1620
	acctatgtaa ccattttaac tctccagtgc actttgccat taaagtctct tcacattg	1678
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5 Met  
gat aac gtc cag ccg aaa ata aac cat cgc ccc ttc tgc ttc agt gtc  
164 Asp Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser Val  
5 10 15  
aaa ggc cac gtc aag atg ctg cgg ctg gat att atc aac tca ctg gta  
212 Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu Val  
20 25 30  
aca aca gta ttc atg ctc atc gta tct gtc gtc gta cta cca gaa  
260 Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Gln  
35 40 45  
acc aca tgc aca gtc ggt gga ggg gtc ttc gca ctt gtc aca gca  
308 Thr Thr Thr Leu Thr Val Gly Gly Val Phe Ala Leu Val Thr Ala  
50 55 60 65  
gta tgc tgt ctt gcc gac ggg gcc ctt att tac cgg aag ctt ctg ttc  
356 Val Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu Phe  
70 75 80  
aat ccc agc ggt cct tac cag caa aag cct gtc cat gaa aaa gaa  
404 Asn Pro Ser Gly Pro Tyr Gln Lys Pro Val His Gln Lys Lys Gln  
85 90 95  
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450 Val Leu  
cattatctg tattctt  
467

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35



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&lt;222&gt; (272)...(841)

&lt;400&gt; 55

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	gggtgctgcg gattgaggtc ccggttccta acgaatctct gctggattgg ccgtaaccct	180
	gtcccccagc gggctcacag ggtctgaagg ccacgcatga ggcaaaggta aagttctgag	240
	ccacccggtg cctccttccc aggactgcaa g atg gag gaa ggc ggg aac cta	292
	Met Glu Glu Gly Gly Asn Leu	
10	1 5	
	gga ggc ctg att aag atg gtc cat cta ctg gtc ttg tca ggt gcc tgg	340
	Gly Gly Leu Ile Lys Met Val His Leu Leu Val Leu Ser Gly Ala Trp	
	10 15 20	
	ggc atg caa atg tgg gtg acc ttc gtc tca ggc ttc ctg ctt ttc cga	388
15	Gly Met Gln Met Trp Val Thr Phe Val Ser Gly Phe Leu Leu Phe Arg	
	25 30 35	
	agc ctt ccc cga cat acc ttc gga cta gtg cag agc aaa ctc ttc ccc	436
	Ser Leu Pro Arg His Thr Phe Gly Leu Val Gln Ser Lys Leu Phe Pro	
	40 45 50 55	
20	ttc tac ttc cac atc tcc atg ggc tgt gcc ttc atc aac ctc tgc atc	484
	Phe Tyr Phe His Ile Ser Met Gly Cys Ala Phe Ile Asn Leu Cys Ile	
	60 65 70	
	ttg gct tca cag cat gct tgg gct cag ctc aca ttc tgg gag gcc agc	532
	Leu Ala Ser Gln His Ala Trp Ala Gln Leu Thr Phe Trp Glu Ala Ser	
25	75 80 85	
	cag ctt tac ctg ctg ttc ctg agc ctt acg ctg gcc act gtc aac gcc	580
	Gln Leu Tyr Leu Leu Phe Leu Ser Leu Thr Leu Ala Thr Val Asn Ala	
	90 95 100	
	cgc tgg ctg gaa ccc cgc acc aca gct gcc atg tgg gcc ctg caa acc	628
30	Arg Trp Leu Glu Pro Arg Thr Thr Ala Ala Met Trp Ala Leu Gln Thr	
	105 110 115	
	gtg gag aag gag cga ggc ctg ggt ggg gag gta cca ggc agc cac cag	676
	Val Glu Lys Glu Arg Gly Leu Gly Gly Glu Val Pro Gly Ser His Gln	
	120 125 130 135	
35	ggc ccc gat ccc tac cgc cag ctg cga gag aag gac ccc aag tac agt	724

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35	Ala Pro Arg Thr Phe Thr Leu Leu Asp Pro Lys Ala Ser Leu Leu Thr gcc cct cgg acc ttt acg ctt ttg gac ccc aag gca tct ctg tta acc 25 30 35 40 45 50 55
30	Gln Ser His Pro Asp Leu Gly Thr Gln Gly Cys Trp Asp Gln Leu Ser cag agc cat cca gac ctg gga act gag ggc tgg gac cag ctc tct 10 15 20
25	Thr Leu Ala Gly Asn Leu Gly Leu Thr Phe Leu Arg Gly Ser Gln Thr acc ctg gct gga aac ctg ggc ctg acc ttc ctc cga ggt tcc cag acc 1 5
20	Met Val Asp Ser Leu Leu Ala Val cagatgccaa agccaaagtc ccaacggacc atg gtg gac agc ctc ctg gca gtc atattggagc caacactcca gatgctacc aaggcctgtcc agatgtccaa gcttccttgc <400> 56 <222> (150)...(1241) <221> CDS <220> <213> Homo sapiens <212> DNA <211> 1256 <210> 56
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10	Leu Gln Ile Arg Ser Leu ctg gaa ata agg agc ctc tagcatgggc cctgcattgct aataaatgct tcttcag 170 175 180
5	Asn Leu Gly Cys Val Leu Ser Asn Gly Leu Cys Leu Ala Gly Leu Ala aat ctg ggc tgc ctg agc aat ggg ctc tgt ctc ggc ctc gcc 155 160 165
	Ala Leu Arg Gln Asn Phe Phe Arg Tyr His Gly Leu Ser Ser Leu Cys gct ctc cgc cag aat ttc ttc cgc tac cat ggg ctg tcc tct ctt tgc 140 145 150
	Gly Pro Asp Pro Tyr Arg Gln Leu Arg Gln Lys Asp Pro Lys Tyr Ser

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	aag gcc ttc ctc aat ggc gcc ctg gat ggg gtc atc ctt gga gac tac	365
	Lys Ala Phe Leu Asn Gly Ala Leu Asp Gly Val Ile Leu Gly Asp Tyr	
	60 65 70	
	ctg agc cgg act cct gag ccc cgg cca tcc ctc agc cac ttg ctg agc	413
5	Leu Ser Arg Thr Pro Glu Pro Arg Pro Ser Leu Ser His Leu Leu Ser	
	75 80 85	
	cag tac tat ggg gct ggg gtg gcc aga gac cca ggg ttc cgc agc aac	461
	Gln Tyr Tyr Gly Ala Gly Val Ala Arg Asp Pro Gly Phe Arg Ser Asn	
	90 95 100	
10	ttc cga cgg cag aac ggt gct gct ctg act tca gcc tcc atc ctg gcc	509
	Phe Arg Arg Gln Asn Gly Ala Ala Leu Thr Ser Ala Ser Ile Leu Ala	
	105 110 115 120	
	cag cag gtg tgg gga acc ctt gtc ctt cta cag agg ctg gag cca gta	557
	Gln Gln Val Trp Gly Thr Leu Val Leu Leu Gln Arg Leu Glu Pro Val	
15	125 130 135	
	cac ctc cag ctt cag tgc atg agc caa gaa cag ctg gcc cag gtg gct	605
	His Leu Gln Leu Gln Cys Met Ser Gln Glu Gln Leu Ala Gln Val Ala	
	140 145 150	
	gcc aat gct acc aag gaa ttc act gag gcc ttc ctg gga tgc ccg gcc	653
20	Ala Asn Ala Thr Lys Glu Phe Thr Glu Ala Phe Leu Gly Cys Pro Ala	
	155 160 165	
	atc cac ccc cgc tgc cgc tgg gga gcg gcg cct tat cgg ggc cgc ccg	701
	Ile His Pro Arg Cys Arg Trp Gly Ala Ala Pro Tyr Arg Gly Arg Pro	
	170 175 180	
25	aag ctg ctg cag ctg ccg ctg gga ttc ttg tac gtg cat cac acc tac	749
	Lys Leu Leu Gln Leu Pro Leu Gly Phe Leu Tyr Val His His Thr Tyr	
	185 190 195 200	
	gtg cct gca cca ccc tgc acg gac ttc acg cgc tgc gca gcc aac atg	797
	Val Pro Ala Pro Pro Cys Thr Asp Phe Thr Arg Cys Ala Ala Asn Met	
30	205 210 215	
	cgc tcc atg cag cgc tac cac cag gac acg caa ggc tgg gga gac atc	845
	Arg Ser Met Gln Arg Tyr His Gln Asp Thr Gln Gly Trp Gly Asp Ile	
	220 225 230	
	ggc tac agt ttc gtg gtg ggc tgc gac ggc tac gtg tac gag gga cgc	893
35	Gly Tyr Ser Phe Val Val Gly Ser Asp Gly Tyr Val Tyr Glu Gly Arg	

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35	caattccctt ctccacatcc aggtcaggtg gcgtttgctg tggcggctag gcccgctg	60
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20	345 Ser Lys Arg Ser Arg Arg Gln Pro Pro Arg Thr Leu Pro Ala Thr tct aag aga tcc aag agg gag cca ccc cca aag acc ctg cca gcc aca	1229
15	330 Trp Pro His Phe Thr Ala Thr Val Lys Pro Arg Pro Ala Arg Ser Val tgg ccg cac ttc acc gcc act gtt aag cca aga cct gcc agt gtc	1181
10	315 Val Arg Thr Asp Cys Pro Gly Asp Ala Leu Phe Asp Leu Arg Thr gtg cgc acc gcc tgc ccc gcc gac gcc ctc ttc gac ctg ctg cgc acc	1133
5	300 Ala Gly Leu Leu Arg Pro Asp Tyr Ala Leu Leu Gly His Arg Gln Leu gcc gcc ctc ctg cgg cca gac tac gcc ctg ctg gcc cgc cag ctg	1085
	285 Ala Ala Leu Arg Thr Val Arg Asp Thr Leu Pro Ser Cys Ala Val Arg gcc gct ctg cgc acc gtc gcc gac acc ctg cgc agt tgt gcc gtc cgc	1037
	265 Phe Gly Val Ala Ile Val Gly Asn Tyr Thr Ala Ala Leu Pro Thr Gln ttc gcc gtc gcc ata gtc gcc aac tac acc gcc gcc ctg ccc acc gag	989
	250 Gly Trp His Trp Val Gly Ala His Thr Leu Gly His Asn Ser Arg Gly ggc tgg cac tgg gtc gcc gcc acc gtc gcc cac acc tcc cgg gcc	941
	245 240 235	

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	gctggagacc tccgcgtg ccccgcgag cctcctgcc tggcccgcg ctgcggtct	120
	gcccgggcgg cagc atg ggt ggc ccc cgg ggc gcg ggc tgg gtg gcg gcg	170
	Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala	
	1 5 10	
5	ggc ctg ctg ctc ggc gcg ggc gcc tgc tac tgc att tac agg ctg acc	218
	Gly Leu Leu Leu Gly Ala Gly Ala Cys Tyr Cys Ile Tyr Arg Leu Thr	
	15 20 25	
	cgg ggt cgg cgg cgg ggc gac cgc gag ctc ggg ata cgc tct tcg aag	266
	Arg Gly Arg Arg Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys	
10	30 35 40	
	tcc gca gaa gac tta act gat ggt tca tat gat gat gtt cta aat gct	314
	Ser Ala Glu Asp Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala	
	45 50 55 60	
	gaa caa ctt cag aaa ctc ctt tac ctg ctg gag tca acg gag gat cct	362
15	Glu Gln Leu Gln Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro	
	65 70 75	
	gta att att gaa aga gct ttg att act ttg ggt aac aat gca gcc ttt	410
	Val Ile Ile Glu Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Ala Phe	
	80 85 90	
20	tca gtt aac caa gct att att cgt gaa ttg ggt ggt att cca att gtt	458
	Ser Val Asn Gln Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val	
	95 100 105	
	gca aac aaa atc aac cat tcc aac cag agt att aaa gag aaa gct tta	506
	Ala Asn Lys Ile Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu	
25	110 115 120	
	aat gca cta aat aac ctg agt gtg aat gtt gaa aat caa atc aag ata	554
	Asn Ala Leu Asn Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile	
	125 130 135 140	
	aag gtg caa gtt ttg aaa ctg ctt ttg aat ttg tct gaa aat cca gcc	602
30	Lys Val Gln Val Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala	
	145 150 155	
	atg aca gaa gga ctt ctc cgt gcc caa gtg gat tca tca ttc ctt tcc	650
	Met Thr Glu Gly Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser	
	160 165 170	
35	ctt tat gac agc cac gta gca aag gag att ctt ctt cga gta ctt acg	698

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35	His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu Lys Asp Phe	200
30	Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe Asn Val	152
25	gcttcgcgag ccgccttgca cctcgcgcgat ccccgacacc cttcttt atg gcg tgc	56
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10	Leu Tyr Asp Ser His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr	746
5	Leu Phe Glu Asn Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala	794
	gag gaa tgc gcc cag aaa ata aga gct tta gct gat cac cat gat gca	842
	Glu Glu Cys Ala Glu Lys Ile Arg Ala Leu Val Asp His His Asp Ala	884
	gag gtc aag gaa aag gtt gta aca ata cca aaa atc tga	
	Glu Val Lys Glu Lys Val Val Thr Ile Ile Pro Lys Ile	
	240 245	
	205 210 215 220	
	Val Glu Pro Thr Phe Thr Glu Gly Ser Leu Phe Phe Leu Leu His Gly	
	gta cag cct act ttc act gaa ggt tca tgc ttt ttc ctg tta cat gga	
	190 195 200	
	cta ttt cag aat ata aag aac tgc ctc aaa ata gaa ggc cat tta gct	
	175 180 185	
	Met Ala Ser	
	1	
	cgc ctg tgc tgc ggc aag cgc ggc tgc ggc atc gtc atc agc	104
	Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile Val Leu Ser	152
	gcc tgg gga gtc atc atg tgc ata atg ctc gga ata ttt ttc aat gtc	
	Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe Asn Val	200
	cat tcc gct gtc atc gtc gac gtc ccc ttc acg gag aaa gat ttt	
	His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu Lys Asp Phe	

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	40	45	50	
	gag aat ggc ccc cag aac ata tac aac ctt tac gag caa gtc agc tac			248
	Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln Val Ser Tyr			
	55	60	65	
5	aac tgt ttc atc gct gca ggc ctt tac ctc ctc ctc gga ggc ttc tct			296
	Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly Gly Phe Ser			
	70	75	80	
	ttc tgc caa gtt cgg ctc aat aag cgc aag gaa tac atg gtg cgc			341
	Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met Val Arg			
10	85	90	95	
	tagggcccc ggcgcgttcc cccgcctccag cccctcctct atttaaagac tccctgcacc			400
	gtgtcaccca ggctgcgtcc cacccttgcc ggcgcctct gtgggactgg gtttcccg			460
	cgagagactg aatcccttct cccatctctg gcacccggcc cccgtggaga gggctgaggg			520
	tggggggctg ttccgtctct ccacccttcg ctgtgtcccg tatctcaata aagagaatct			580
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	Met Val Gly Pro Ala Pro Arg Arg Arg			
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	ctg cgg ccg ctg gca gcg ctg gcc ctg gtc ctg gcg ctg gcc ccg ggg			99
30	Leu Arg Pro Leu Ala Ala Leu Ala Leu Val Leu Ala Leu Ala Pro Gly			
	10	15	20	25
	ctg ccc aca gcc cgg gcc ggg cag aca ccg cgc cct gcc gag cgg ggg			147
	Leu Pro Thr Ala Arg Ala Gly Gln Thr Pro Arg Pro Ala Glu Arg Gly			
	30	35	40	
35	ccc cca gtg cgg ctt ttc acc gag gag gag ctg gcc cgc tat gcc ggg			195

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640	gcaggagagac actaggtgct gaatctcctg caaaactggc tgcctggagg cccctgagcca	
	170	
25	Asp Glu Phe	
580	gat gag ttc tgatgttccc cctgcaggag caggtcttg gagcgctgag	
	155	160
	Pro Asn Leu Asp Phe Lys Pro Glu Asp Glu Pro His Phe Asp Ile Lys	165
531	cct aac ctg gac ttc aag cct gaa gac cag ccc cat ttt gac atc aag	
	140	145
20	Pro Ile Val Gly Tyr Thr Ala Arg Arg Ile Leu Asn Glu Asp Gly Ser	150
483	ccc atc gtc ggc tac aac act gcc cgg aga att ctc aat gag gat ggc agc	
	125	130
	Ileu Glu Ala Leu Asp Glu Val Phe Thr Lys Val Tyr Lys Ala Lys Tyr	135
435	ctg gag gcc ctg gat gag gtc ttc acc aaa gtg tac aaa gcc aac tac	
	110	115
	Asp Pro Ala Asp Leu Thr His Asp Thr Thr Gly Leu Thr Ala Lys Glu	120
387	gat cct gca gac ctc acc cat gac act acg ggt ctc acg gcc aag gaa	
	90	95
	Ala Leu Thr Gly Lys Asp Ser Thr Arg Gly Val Ala Lys Met Ser Leu	100
339	gcc ttg acg ggg aag gac tcc act aga ggg gta gcc aag atg tcc ttg	
	75	80
	Asp Val Thr Ser Gly Lys Glu Phe Tyr Gly Arg Gly Ala Pro Tyr Asn	85
291	gat gtc acc tcc gga aag gag ttt tat gga cga gga gcc ccc tac aat	
	60	65
	Glu Glu Glu Asp Glu Pro Ile Tyr Leu Ala Val Lys Gly Val Val Phe	70
243	gag gag gaa gat cag ccc atc tac ttg gca gtg aag gga gtg ttg ttt	
	45	50
	Pro Pro Val Arg Leu Phe Thr Glu Glu Leu Ala Arg Tyr Gly Gly	55



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&lt;222&gt; (127)...(489)

&lt;400&gt; 60

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5	gccaaccgtg ggcgagctct ggggtgtgagg ggggcctggc gcggcgctcc gctgtgtcag	120
	cgtgtt atg atg ccg tcc cgt acc aac ctg gct act gga atc ccc agt	168
	Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser	
	1 5 10	
	agt aaa gtg aaa tat tca agg ctc tcc agc aca gac gat ggc tac att	216
10	Ser Lys Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile	
	15 20 25 30	
	gac ctt cag ttt aag aaa acc cct cct aag atc cct tat aag gcc atc	264
	Asp Leu Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile	
	35 40 45	
15	gca ctt gcc act gtg ctg ttt ttg att ggc gcc ttt ctc att att ata	312
	Ala Leu Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile	
	50 55 60	
	ggc tcc ctc ctg ctg tca ggc tac atc agc aaa ggg ggg gca gac cgg	360
	Gly Ser Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg	
20	65 70 75	
	gcc gtt cca gtg ctg atc att ggc att ctg gtg ttc cta ccc gga ttt	408
	Ala Val Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe	
	80 85 90	
	tac cac ctg cgc atc gct tac tat gca tcc aaa ggc tac cgt ggt tac	456
25	Tyr His Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr	
	95 100 105 110	
	tcc tat gat gac att cca gac ttt gat gac tagcaccac ccca	500
	Ser Tyr Asp Asp Ile Pro Asp Phe Asp Asp	
	115 120	
30	tagctgagga ggagtcacag tggaactgtc ccagctttaa gatatttagc agaaactata	560
	gctgaggact aaggaattct gcagcttgca gatgtttaag aaaataatgg ccagattttt	620
	tgggtccttc ccaaagatgt taagtgaacc tacagtttagc taattaggac aagctctatt	680
	tttcatccct gggccctgac aagtttttcc acaggaatat gtatcatgga agaatagagg	740
	ttattctgta atggaaaagt gttgcctgcc accaccctct gtagagctga gcattttttt	800
35	taaatagtct tcattgcca tttgttcttg tagcaaatgg aacaatgtgg tatggcta	860

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920      ttcttat taagtatt atttaaaa tctctagta tttatctg tacaattac  
980      cttaccatca tgtccagtg gaagaccat gtaaatcaa agatcagtg gttcatctgt  
1040      aatatatttt ttacttgct tcttaactgac agcaaacagg aatttttta tccctgagag  
1100      caagtttca aatgttaaat acttccctcg tttaacagtc cttggaecat tctgatacag  
1160      ttcaaccagta ggttggaag catataattt gcatcatitt gttcccttgta aatcaagatg  
1220      ttctgcagat tattcctta acggccggac ttcttgctgt ttccctaaaga aacatgtagt  
1280      ggttatatt tagagtatt agccgtattg ctgagacct gtagtatgac atcatctgc  
1340      tcatgatcc aagatcagc ctgatatcct agaggaactag atcaacttag ttgatctca  
1400      tttttagct tgcataaagt gacttatc ccaaaagaaat taatatgtg aatcccaat  
1425      cctagaata aatgagta acttc

<210> 61  
<211> 307  
<212> PRT  
<213> Homo sapiens

Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp Gly Leu  
1 5 10 15

Pro Leu Ser Ala Ser Thr Asp Tyr Glu Glu Ser Thr Gly Met Glu Glu  
20 25 30

Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Glu Leu Pro  
35 40 45

Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe Ile Ser  
50 55 60

Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr Pro Asn  
65 70 75 80

Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Glu Lys Glu Phe Ile Thr  
85 90 95

Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr Cys Phe  
100 105 110

Ile Glu Phe Asp Asn Phe Ile Glu Arg Thr Lys Glu Arg Tyr Asn Asn  
115 120 125

Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Glu Thr Glu  
130 135 140

35

30

25

20

15

10

5

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Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu Gly Ser  
 145                      150                      155                      160  
 Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly Ala Gly  
                          165                      170                      175  
 5    Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu Ser Gly  
                          180                      185                      190  
 Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn Leu Ile  
                          195                      200                      205  
 Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly Asp Asp  
 10                      210                      215                      220  
 Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys Leu Tyr  
 225                      230                      235                      240  
 Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val Lys Ser  
                          245                      250                      255  
 15    Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu Tyr Glu  
                          260                      265                      270  
 Leu Arg Asn Leu Trp Gln Leu Phe Phe His Val Thr Val Gly Ala Phe  
                          275                      280                      285  
 Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala Pro Asp  
 20                      290                      295                      300  
 Tyr Asp Val  
 305  
  
 <210> 62  
 25    <211> 183  
       <212> PRT  
       <213> Homo sapiens  
  
 <400> 62  
 30    Met Thr Ala Gln Gly Gly Leu Val Ala Asn Arg Gly Arg Arg Phe Lys  
          1                      5                      10                      15  
 Trp Ala Ile Glu Leu Ser Gly Pro Gly Gly Gly Ser Arg Gly Arg Ser  
                          20                      25                      30  
 Asp Arg Gly Ser Gly Gln Gly Asp Ser Leu Tyr Pro Val Gly Tyr Leu  
 35                      35                      40                      45

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35	65	70	75	80
30	50	55	60	
25	63			
20	63			
15	180			
10	115	120	125	
5	65	70	75	80
	50	55	60	
	1	5	10	15
	20	25	30	
	35	40	45	
	50	55	60	
	65	70	75	80

Asp Lys Gln Val Pro Asp Thr Ser Val Gln Gln Thr Asp Arg Ile Leu  
 Val Gln Lys Arg Cys Trp Asp Ile Ala Leu Gly Pro Leu Lys Gln Ile  
 Pro Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr Ile Ser Ile  
 Phe Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro Ile Gln Ala  
 Leu Met Ala Ile Ser Ala Thr Phe Lys Met Leu Gln Ser Ser Ser Gln  
 Lys Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu Met Gly Leu  
 Ala Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu Pro Thr His  
 Ala Ser Asp Trp Leu Ala Phe Ile Gln Pro Pro Gln Arg Met Gln Phe  
 Ser Gly Gly Leu Leu Leu  
 Met Arg Ala Leu Pro Gly Leu Leu Gln Ala Arg Ala Arg Thr Pro Arg  
 Leu Leu Leu Leu Gln Cys Leu Leu Ala Ala Arg Pro Ser Ser Ala  
 Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro Pro Leu Arg Gln  
 Gln Ile Met Ala Asn Asn Phe Ser Leu Gln Ser His Asn Ile Ser Leu  
 Thr Gln His Ser Ser Met Pro Val Gln Lys Asn Ile Thr Leu Gln Arg

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Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr Ser Gly Asp Leu  
                             85                            90                            95  
 Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu Gln Leu Glu Asn  
                             100                            105                            110  
 5 Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr Thr Gln Tyr Arg  
                             115                            120                            125  
 Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr Ser Cys Phe Phe  
                             130                            135                            140  
 Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe Lys Val Pro Glu  
 10 145                            150                            155                            160  
 Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val Gly Asp Ser Thr  
                             165                            170                            175  
 Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu Asn Trp Thr Trp  
                             180                            185                            190  
 15 Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly Val Gln Met Asn  
                             195                            200                            205  
 Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr Lys Leu Lys Ile  
                             210                            215                            220  
 Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp Cys Arg Ala Leu  
 20 225                            230                            235                            240  
 Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu Val Val Leu Ser  
                             245                            250                            255  
 Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val Ala Glu Val Ile  
                             260                            265                            270  
 25 Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr Thr Gln Lys Lys  
                             275                            280                            285  
 Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln Ile Glu Gln Leu  
                             290                            295                            300  
 Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val Pro Arg His Arg  
 30 305                            310                            315                            320  
 Lys Asn Glu Ser Leu Gly Gln  
                             325

&lt;210&gt; 64

35 &lt;211&gt; 223

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<212> PRT

<213> Homo sapiens

<400> 64

5 Met Lys Phe Val Pro Cys Leu Leu Val Thr Leu Ser Cys Leu Gly

1

5

10

15

Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Gln

20

25

30

Phe His Phe Gln Thr Gly Arg Asp Ser Cys Thr Met Arg Pro Ser

10

35

40

45

Ser Leu Gly Gln Gly Ala Gly Gln Val Trp Leu Arg Val Asp Cys Arg

50

55

60

Asn Thr Asp Gln Thr Tyr Trp Cys Gln Tyr Arg Gly Gln Pro Ser Met

65

70

75

80

15

Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala Leu

85

90

95

Gln Gln Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val Leu

100

105

110

Arg Pro Ser Val Cys Arg Gln Ala Gly Pro Gln Ala His Met Gln Gln

20

115

120

125

Val Thr Ser Ser Ser Leu Lys Gly Ser Pro Gln Pro Asn Gln Pro Gln

130

135

140

Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr Gln

145

150

155

Ala Thr Gln Leu Gly Lys Asp Ser Met Gln Gln Leu Gly Lys Ala Lys

165

170

175

Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg Pro

180

185

190

Gly Gly Asn Gln Gln Ala Lys Lys Lys Ala Trp Gln His Cys Trp Lys

30

195

200

205

Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly

210

215

220

35 <210> 65

<211> 48

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&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 65

5 Met Arg Leu Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg  
 1 5 10 15  
 Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys  
 20 25 30  
 Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser  
 10 35 40 45

&lt;210&gt; 66

&lt;211&gt; 371

&lt;212&gt; PRT

15 &lt;213&gt; Homo sapiens

&lt;400&gt; 66

Met Ala Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val  
 1 5 10 15  
 20 Thr Gly Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met  
 20 25 30  
 Ala Glu Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe  
 35 40 45  
 Leu Gln Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala  
 25 50 55 60  
 Phe Tyr Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val  
 65 70 75 80  
 Asp Pro Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu  
 85 90 95  
 30 Cys Asp Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr  
 100 105 110  
 Ser Ala Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Ile Phe Thr  
 115 120 125  
 Gly Leu Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln  
 35 130 135 140

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35	<210> 67	<211> 90	<212> PRT	<213> Homo sapiens
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	355	360	365	
	340	345	350	
25	325	330	335	
	305	310	315	
	290	295	300	
20	275	280	285	
	260	265	270	
15	245	250	255	
	225	230	235	
	210	215	220	
10	195	200	205	
	180	185	190	
5	165	170	175	
	145	150	155	
	160			



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&lt;400&gt; 67

Met Phe His Gln Ile Trp Ala Ala Leu Leu Tyr Phe Tyr Gly Ile Ile  
 1 5 10 15  
 5 Leu Asn Ser Ile Tyr Gln Cys Pro Glu His Ser Gln Leu Thr Thr Leu  
 20 25 30  
 Gly Val Asp Gly Lys Glu Phe Pro Glu Val His Leu Gly Gln Trp Tyr  
 35 40 45  
 Phe Ile Ala Gly Ala Ala Pro Thr Lys Glu Glu Leu Ala Thr Phe Asp  
 10 50 55 60  
 Pro Val Asp Asn Ile Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met  
 65 70 75 80  
 Gln Leu His Leu Arg Ala Thr Ile Arg Met  
 85 90

15

&lt;210&gt; 68

&lt;211&gt; 499

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

20

&lt;400&gt; 68

Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu  
 1 5 10 15  
 Ala Ile Gly Ala Ala Ile Phe Glu Val Leu Glu Glu Pro His Trp Lys  
 25 20 25 30  
 Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu  
 35 40 45  
 Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val  
 50 55 60  
 30 Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe  
 65 70 75 80  
 Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile  
 85 90 95  
 Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg  
 35 100 105 110

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5	Leu phe cys Val phe tyr gly leu phe gly Val pro leu cys leu thr	115	120	125
	trp ile ser ala leu gly lys phe phe gly arg ala lys arg leu	130	135	140
	gly gln phe leu thr lys arg gly Val ser leu arg lys ala gln ile	145	150	155
10	thr cys thr Val ile phe ile Val trp gly Val leu Val his leu Val	165	170	175
	ile pro pro phe Val phe met Val thr gln gly trp asn tyr ile gln	180	185	190
	gly leu tyr tyr ser phe ile thr ile ser thr ile gly phe gly asp	195	200	205
15	phe Val ala gly Val asn pro ser ala asn tyr his ala leu tyr arg	210	215	220
	tyr phe Val gln leu trp ile tyr leu gly leu ala trp leu ser leu	225	230	235
	phe Val asn trp lys Val ser met phe Val gln Val his lys ala ile	245	250	255
20	lys lys arg arg arg arg lys gln ser phe gln ser ser pro his	260	265	270
	ser arg lys ala leu gln Val lys gly ser thr ala ser lys asp Val	275	280	285
	asn ile phe ser phe leu ser lys lys gln thr tyr asn asp leu	290	295	300
25	ile lys gln ile gly lys lys ala met lys thr ser gly gly gly gln	305	310	315
	thr gly pro gly pro gly leu gly pro gln gly gly gly leu pro ala	325	330	335
	leu pro pro ser leu Val pro leu Val Val tyr ser lys asn arg Val	340	345	350
30	pro thr leu gln gln Val ser gln thr leu arg ser lys gly his Val	355	360	365
	ser arg ser pro asp gln ala Val ala arg ala pro gln asp ser	370	375	380
	ser pro ala pro gln Val phe met asn gln leu asp arg ile ser gln			

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385                      390                      395                      400  
 Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln  
                          405                      410                      415  
 Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu  
 5                      420                      425                      430  
 Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser  
                          435                      440                      445  
 Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe  
                          450                      455                      460  
 10 Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser  
                          465                      470                      475                      480  
 Val Pro Tyr Glu Gln Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro  
                          485                      490                      495  
 Lys Gly Thr  
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 <210> 69  
 <211> 106  
 <212> PRT  
 20 <213> Homo sapiens  
  
 <400> 69  
 Met Ala Ser Ser Gly Ala Gly Asp Pro Leu Asp Ser Lys Arg Gly Glu  
       1                      5                      10                      15  
 25 Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr Arg Glu Lys Leu Thr Pro  
                          20                      25                      30  
 Glu Gln Leu His Ser Met Arg Gln Ala Glu Leu Ala Gln Trp Gln Lys  
                          35                      40                      45  
 Val Leu Pro Arg Arg Arg Thr Arg Asn Ile Val Thr Gly Leu Gly Ile  
 30                      50                      55                      60  
 Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr Thr Phe Tyr Ser Ile Ser  
                          65                      70                      75                      80  
 Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp Glu Ala Lys Ala Ala Arg  
                          85                      90                      95  
 35 Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser

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35	<210> 71	<211> 921	<212> DNA	<213> Homo sapiens	<400> 71
30	<210> 71				
	145				150
	Ala gln gln Asp His pro gln				
25	130	135	140		
	Gly gln Asp Leu His Ser Thr Val Tyr gln Val Ile gln His Ile pro				
	115	120	125		
	Val Ser Arg Ile pro Ser Arg Ser Val pro Ala Ser Asp Cys Val Ser				
20	100	105	110		
	Asp Asp phe Gly Ile Tyr gln phe Val Ala phe pro Asp Val Ser Gly				
	85	90	95		
	Thr gln Tyr Arg Lys Ala gln Thr phe Ser Gly His gln Asp Ala Leu				
	65	70	75		80
	Tyr gln pro Tyr Lys Val Ile Lys gln Lys Leu gln Gly Arg pro gln				
15	50	55	60		
	Ser Leu phe Leu Ile Ile Ser Met Cys Leu Leu phe Leu Trp Lys Lys				
	35	40	45		
	Ala gln Lys Gly Lys Ser Leu Ser pro Leu Ala Ser Ile Thr Gly Ile				
10	20	25	30		
	Gln Thr His phe Thr Val Ile Ile Thr Ser Val Gly Leu gln Lys Leu				
	1	5	10	15	
	Met Asp Tyr Val Cys Cys Ala Tyr Asn Asn Ile Thr Gly Arg gln Asp				
5	<210> 70	<211> 152	<212> PRT	<213> Homo sapiens	<400> 70
	100				105

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	tctactgatt atgaacaaag cacaggaatg caggagtga gaaagtattt taaaatgett	120
	tcgaggaaac ttgtccaact tcctgataga tgtacactga aaactggaca ttataacatt	180
	aattttatta gctctctggg agtgagctac atgatgttgt gcaactgaaa ttacccaaat	240
5	gttctcgctt tctctttcct ggatgagctt cagaaggagt tcattactac ttataacatg	300
	atgaagacaa ataactgctgt cagaccatac tgtttcattg aatttgataa cttcattoag	360
	aggaccaagc agcgatataa taatcccagg tctctttcaa caaagataaa tctttctgac	420
	atgcagacgg aaatcaagct gaggcctcct tatcaaatTT ccatgtgcga actgggggtca	480
	gccaatggag tcacatcage attttctgtt gactgtaaag gtgctggtaa gattttctct	540
10	gctcaccage gactggaacc agcaactctg tcagggattg taggatttat ccttagtctt	600
	ttatgtggag ctctgaattt aattcgaggc tttcatgcta tagaaagtct cctgcagagt	660
	gatggtgatg attttaatta catcattgca tttttccttg gaacagcagc ctgcctttac	720
	cagtgttatt tacttgtcta ctacaccggc tggcggaatg tcaaatcttt tttgactttt	780
	ggcttaatct gtctatgcaa catgtatctc tatgaactgc gcaacctctg gcagcttttc	840
15	tttcatgtga ctgtgggagc atttgttaca ctacagatct ggctaaggca agcccagggc	900
	aaggctcccc attatgatgt c	921
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	<211> 549	
20	<212> DNA	
	<213> Homo sapiens	
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25	ctaagcgggc ctggaggagg cagcaggggt cgaagtgacc ggggcagtgg ccaggagac	120
	tcgctctacc cagtcggtta cttggacaag caagtgcctg ataccagcgt gcaagagaca	180
	gaccggatcc tgggtggagaa gcgctgctgg gacatcgcct tgggtccctt caaacagatt	240
	cccatgaatc tcttcatcat gtacatggca ggcaatacta tctccatctt ccctactatg	300
	atggtgtgta tgatggcctg gcgacccatt caggcaactta tggccatttc agccactttc	360
30	aagatgttag aaagttcaag ccagaagttt cttcagggtt tgggtctatct cattgggaac	420
	ctgatgggtt tggcattggc tgtttacaag tgccagtcca tgggactgtt acctacacat	480
	gcateggatt ggtagcctt cattgagccc cctgagagaa tggagttoag tgggtggagga	540
	ctgcttttg	549
35	<210> 73	

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 ttacagagtc cacccttcag agagagagata atggcagagata accttccttc gtagagagtc  
 180  
 120  
 60  
 10  
 240  
 300  
 360  
 420  
 480  
 540  
 600  
 660  
 720  
 780  
 840  
 900  
 960  
 981  
 aacatatac tgaactgagaca tctcagatcag cagatagagaa aatatatac tttagagag  
 cctctatag taatatctcac atgcagagtc aacacatcgg gggatttga tgcagatagat  
 gtcacttggg aaaaagatgg tgaacacact agagatatat atcttgcag tgcacacagga  
 agcaccttgc atcacccata caggttcacac atcatataca gcaaacacacat gggagagttat  
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 cttcataggga aaaaacagcc attgatctct tacgttagggg atctacactgt cttgacactgt  
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 720  
 780  
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 900  
 960  
 981  
 aatgttcaaa attgttttc tttaaatgg accctgttcaa gtagtcaatgg gtagtcaatgg  
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 aagcttgaaga taacacacac tttagagagaa gattggagat cttacatgag cagtgcacat  
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 840  
 900  
 960  
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 aaaaatagagt cctcggggca g  
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 <211> 669  
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	ggaccccagg cccatattgca gcaggtgact tccagcctca agggcagccc agagcccaac	420
	cagcagcctg aggtctgggac gccatctctg aggcccaagg ccacagtga actcacagaa	480
	gcaacacagc tgggaaagga ctcgatggaa gagctgggaa aagccaaacc caccacccga	540
	cccacagcca aacctaccca gcctggaccc agggccggag ggaatgagga agcaaagaag	600
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	ttccgaggg	669
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	<211> 144	
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	<213> Homo sapiens	
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	ctcaagttcc agatttgtgt ttcc	144
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	<211> 1113	
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	<213> Homo sapiens	
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	gagcacagct tccagcatcc ctctctccag gcagtgggca tgttcctggg agaattctcc	180
	tgcctggctg cttctacct cctccgatgc agagctgcag ggcaatcaga ctccagcgta	240
	gacccccagc agcccttcaa ccctcttctt ttcttgcccc cagcgtcttg tgacatgaca	300
	gggaccagcc tcatgtatgt ggctctgaac atgaccagtg cctccagctt ccagatgctg	360
30	cggggtgcag tgatcatatt cactggcctg ttctcggtgg ccttcctggg ccggaggctg	420
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	gctgacctcc tgagcaagca cgacagtcag cacaagctca gogaagtgat cacaggggac	540
	ctgttgatca tcatggccca gatcatcggt gccatccaga tggctgtaga ggagaagttc	600
	gtctacaaac acaatgtgca ccaactgcgg gcagtggca ctgagggcct ctttggtttt	660
35	gtgatcctct ccctgctgct ggtgcccatt tactacatcc ccgccggctc ctccagcgga	720

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780 540 360 300 240 180 120 60  
aaaccctcgtg ggaacactga ggaatgcatg gaagccctc gcaaggtctg ccaagagccg  
ctcaatcgcg tggcaactgct gggaacatc gggaacatcgg cctcctccaa cctcgcagagc  
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gttgtcatct gggaacatgag cctcgcacatg ggatcgggaag cctcgcacatg acatgagatc  
cctcgcctcc tcatatccct tataggaact gccctcctaca atgggctaca cgtcgcgtg  
ctgggcgcgc tgcacagggg cgggcgcctg gcaagaggaag gcgagagga ggaactcgtg  
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1113 1080 1020 960 900 840 780

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20

<210> 78

<211> 1497

<212> DNA

<213> Homo sapiens

25

<400> 78

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cagaaagctcg atcctgcaca ggaagtcccg tgcctcgtgc aggaagggcct ggaacaaagatc  
ctagaaggtg tcatctgactg tgcagagacag ggtgtggtgcaa tcaacagggga ccaagacctc  
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gtattcatgg tgactgaggg gtggaactac atcgagggcc tctactactc cttcatcacc 600  
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 gccctgtacc gctacttcgt ggagctctgg atctacttgg ggetggcctg gctgtccett 720  
 tttgtcaact ggaagggtgag catgtttgtg gaagtccaca aagccattaa gaagcggcgg 780  
 5 cggcgacgga aggagtcctt tgagagctcc ccacactccc ggaaggccct gcaggtgaag 840  
 gggagcacag cctccaagga cgtcaacatc ttcagctttc tttccaagaa ggaagagacc 900  
 tacaacgacc tcatcaagca gatcgggaag aaggccatga agacaagcgg ggggtggggag 960  
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 gaatgcgagc catgggacgc ccaggactac caccactca tcttcaggga cgccagcatc 1260  
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 gacaacttgg caggggagga gagccccag cagggggctg aagccaaggc gccctgaac 1380  
 15 atgggcgagt tcccctcctc ctccgagtc accttcacca gcactgagtc tgagctctct 1440  
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&lt;210&gt; 79

&lt;211&gt; 318

20 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 79

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 gcggagcttg ccagtgga gaaggtccta ccacggcggc gaaccggaa catcgtgacc 180  
 ggcctaggca tcggggccct ggtgttggtt atttatggtt acaccttcta ctcgatttcc 240  
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30

&lt;210&gt; 80

&lt;211&gt; 456

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

35

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35	65	70	75	Ile Ser Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Gln Asn Tyr
				att agc tct ctg gga gtg agc tac atg atg tgc act gaa aat tac
30	50	55	60	Leu Pro Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe
				ctt cct gat aga tgt aca ctg aaa act gga cat tat aac att aat ttt
25	15	20	25	Gly Leu Pro Leu Ser Ala Ser Thr Asp Tyr Gln Ser Thr Gly Met
				gga ctg cca ctt tct gct tct act gat tat gaa caa agc aca gga atg
20	1	5	10	Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp
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5	<400> 80	<210> 81	<211> 1436	atataatgaat ttgttgcctt tccagatgtt tctgtgttcc caggtatccc aagcaggtct
				atataatgaat ttgttgcctt tccagatgtt tctgtgttcc caggtatccc aagcaggtct

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	cca aat gtt ctc gcc ttc tct ttc ctg gat gag ctt cag aag gag ttc	347
	Pro Asn Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Gln Lys Glu Phe	
	80 85 90	
5	att act act tat aac atg atg aag aca aat act gct gtc aga cca tac	395
	Ile Thr Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr	
	95 100 105 110	
	tgt ttc att gaa ttt gat aac ttc att cag agg acc aag cag cga tat	443
	Cys Phe Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr	
	115 120 125	
10	aat aat ccc agg tct ctt tca aca aag ata aat ctt tct gac atg cag	491
	Asn Asn Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln	
	130 135 140	
	acg gaa atc aag ctg agg cct cct tat caa att tcc atg tgc gaa ctg	539
	Thr Glu Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu	
15	145 150 155	
	ggg tca gcc aat gga gtc aca tca gca ttt tct gtt gac tgt aaa ggt	587
	Gly Ser Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly	
	160 165 170	
	gct ggt aag att tct tct gct cac cag cga ctg gaa cca gca act ctg	635
20	Ala Gly Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu	
	175 180 185 190	
	tca ggg att gta gga ttt atc ctt agt ctt tta tgt gga gct ctg aat	683
	Ser Gly Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn	
	195 200 205	
25	tta att cga ggc ttt cat gct ata gaa agt ctc ctg cag agt gat ggt	731
	Leu Ile Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly	
	210 215 220	
	gat gat ttt aat tac atc att gca ttt ttc ctt gga aca gca gcc tgc	779
	Asp Asp Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys	
30	225 230 235	
	ctt tac cag tgt tat tta ctt gtc tac tac acc ggc tgg cgg aat gtc	827
	Leu Tyr Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val	
	240 245 250	
	aaa tct ttt ttg act ttt ggc tta atc tgt cta tgc aac atg tat ctc	875
35	Lys Ser Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu	

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255 260 265 270

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Tyr Gln Leu Arg Asn Leu Trp Gln Leu Phe Phe His Val Thr Val Gly

275 280 285

gca ttt gtc aca cta cag atc tgg cta agg caa gcc cag ggc aag gct  
Ala Phe Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala

290 295 300

ccc gat tat gat gtc tgaaccatc ctccagatct attgacctgg ctcc  
Pro Asp Tyr Asp Val

305 10

aggaggatata ggaaggagaca tatcatatcat gcaactgttgat gaagaaagctg tccccccacag  
aggagaaagct ctgcttctct tctctccaaac ttctcttttt taataatcagcc atgatgtgccc

1140 tctcagagagaa tgttggccat gaaactatca ttcagagagag

1200 tgttgagcatg gaagagagctc ctccagagagaa tctcagagagaa

1260 gaggaggattt ctctcttcaaa ggcacataca gttggagaaac agtccatatgc cattggaaat

1320 ctggccagc agtccctgat cctccctgaa gattccagaa aatagatgtg gtaattgctct

1380 gaggagccag caggagagaa tctaacaaact gatttggcc tttgtgagagca ttatgataga

1436 ccaatataaa agctggcagaa attggaagt ttatgtttta aataaatgac tgtgat

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60 110 Met Thr Ala Gln Gly Leu Val

1

5

gct aac cga ggc cgg cgc ttc aag tgg gcc att gag cta aag cct

158 Ala Asn Arg Gly Arg Arg Phe Lys Trp Ala Ile Gln Leu Ser Gly Pro

10

15

20

35 gga gga ggc aag ggc agt cga agt gac cgg ggc agt ggc cag gga gac

206

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	Gly Gly Gly Ser Arg Gly Arg Ser Asp Arg Gly Ser Gly Gln Gly Asp	
	25 30 35 40	
	tcg ctc tac cca gtc ggt tac ttg gac aag caa gtg cct gat acc agc	254
	Ser Leu Tyr Pro Val Gly Tyr Leu Asp Lys Gln Val Pro Asp Thr Ser	
5	45 50 55	
	gtg caa gag aca gac cgg atc ctg gtg gag aag cgc tgc tgg gac atc	302
	Val Gln Glu Thr Asp Arg Ile Leu Val Glu Lys Arg Cys Trp Asp Ile	
	60 65 70	
	gcc ttg ggt ccc ctc aaa cag att ccc atg aat ctc ttc atc atg tac	350
10	Ala Leu Gly Pro Leu Lys Gln Ile Pro Met Asn Leu Phe Ile Met Tyr	
	75 80 85	
	atg gca ggc aat act atc tcc atc ttc cct act atg atg gtg tgt atg	398
	Met Ala Gly Asn Thr Ile Ser Ile Phe Pro Thr Met Met Val Cys Met	
	90 95 100	
15	atg gcc tgg cga ccc att cag gca ctt atg gcc att tca gcc act ttc	446
	Met Ala Trp Arg Pro Ile Gln Ala Leu Met Ala Ile Ser Ala Thr Phe	
	105 110 115 120	
	aag atg tta gaa agt tca agc cag aag ttt ctt cag ggt ttg gtc tat	494
	Lys Met Leu Glu Ser Ser Ser Gln Lys Phe Leu Gln Gly Leu Val Tyr	
20	125 130 135	
	ctc att ggg aac ctg atg ggt ttg gca ttg gct gtt tac aag tgc cag	542
	Leu Ile Gly Asn Leu Met Gly Leu Ala Leu Ala Val Tyr Lys Cys Gln	
	140 145 150	
	tcc atg gga ctg tta cct aca cat gca tgc gat tgg tta gcc ttc att	590
25	Ser Met Gly Leu Leu Pro Thr His Ala Ser Asp Trp Leu Ala Phe Ile	
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	gag ccc cct gag aga atg gag ttc agt ggt gga gga ctg ctt ttg tgaac	640
	Glu Pro Pro Glu Arg Met Glu Phe Ser Gly Gly Gly Leu Leu Leu	
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30	atgagaaagc agcgccctggt ccctatgtat ttgggtotta ttacatcct tctttaagcc	700
	cagtggctcc tcagcatact cttaaactaa tcacttatgt taaaaagaac caaaagactc	760
	ttttctccat ggtggggtga caggctctag aaggacaatg tgcattattac gacaaacaca	820
	aagaaactat accataaccc aaggetgaaa ataatgtaga aaactttatt tttgtttcca	880
	gtacagagca aaacaacaac aaaaaaacat aactatgtaa acaagagaat aactgctgct	940
35	aatcaagaa ctggtgcagc atctcctttc aataaattaa atggttgaga acaatgc	997

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	gggaactctg accaccgccg cggcgagctg agggagagct ctcacagagc gccacagcgcg	120
15	accctctggc gcc atg cgc gcc ctc gcc ccc gcc ctc gtc ggc gcc agc gcc	169
	Met Arg Ala Leu Pro Gly Leu Leu Glu Ala Arg Ala	
	1	5
20	15	20
	cca agc tcg gcc gac ggc agt gcc cca gat tcg cct ttt acc agt cca	265
	Pro Ser Ser Ala Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro	
25	30	35
	cct ctc aga gaa gaa ata atg gca aat aac ttt tcc ttg gag agt cat	313
	Pro Leu Arg Glu Ile Met Ala Asn Asn Phe Ser Leu Glu Ser His	
30	45	50
	aac ata tca ctg act gaa cat tct agt atg cca gta gaa aaa aat atc	361
	Asn Ile Ser Leu Thr Glu His Ser Ser Met Pro Val Glu Lys Asn Ile	
35	65	70
	act tta gaa agc cct tct aat gta aat ctc aca tgc cag ttc aca aca	409
	Thr Leu Glu Arg Pro Ser Asn Val Asn Leu Thr Cys Glu Phe Thr Thr	
40	80	85
	tct ggg gat ttg aat gca gta aat gtc act tgg aaa aaa gat ggt gaa	457
	Ser Gly Asp Leu Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu	
45	95	100
	caa ctt gag aat aat tat ctt gtc agt gca aca gga acc ttg tat	505
	Gln Leu Glu Asn Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr	

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	110	115	120	
	acc caa tac agg ttc acc atc att aat agc aaa caa atg gga agt tat			553
	Thr Gln Tyr Arg Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr			
	125	130	135	140
5	tct tgt ttc ttt cga gag gaa aag gaa caa agg gga aca ttt aat ttc			601
	Ser Cys Phe Phe Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe			
	145	150	155	
	aaa gtc cct gaa ctt cat ggg aaa aac aag cca ttg atc tct tac gta			649
	Lys Val Pro Glu Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val			
10	160	165	170	
	ggg gat tct act gtc ttg aca tgt aaa tgt caa aat tgt ttt cct tta			697
	Gly Asp Ser Thr Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu			
	175	180	185	
	aat tgg acc tgg tac agt agt aat ggg agt gta aag gtt cct gtt ggt			745
15	Asn Trp Thr Trp Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly			
	190	195	200	
	gtt caa atg aat aaa tat gtg atc aat gga aca tat gct aac gaa aca			793
	Val Gln Met Asn Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr			
	205	210	215	220
20	aag ctg aag ata aca caa ctt ttg gag gaa gat ggg gaa tct tac tgg			841
	Lys Leu Lys Ile Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp			
	225	230	235	
	tgc cgt gca cta ttc caa tta ggc gag agt gaa gaa cac att gag ctt			889
	Cys Arg Ala Leu Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu			
25	240	245	250	
	gtg gtg ctg agc tat ttg gtg ccc ctc aaa cca ttt ctt gta ata gtg			937
	Val Val Leu Ser Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val			
	255	260	265	
	gct gag gtg att ctt tta gtg gcc acc att ctg ctt tgt gaa aag tac			985
30	Ala Glu Val Ile Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr			
	270	275	280	
	aca caa aag aaa aag aag cac tca gat gag ggg aaa gaa ttt gag cag			1033
	Thr Gln Lys Lys Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln			
	285	290	295	300
35	att gaa cag ctg aaa tca gat gat agc aat ggt ata gaa aat aat gtc			1081

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Ile Gln Gln Leu Lys Ser Asp Ser Asn Gly Ile Gln Asn Val  
 305 310 315  
 1130 ccc agg cat aga aaa aat gag tct ctg ggc cag tgaatacaaa acatca  
 Pro Arg His Arg Lys Asn Gln Ser Leu Gly Gln  
 320 325

5  
 10  
 15  
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 1250 taagagccctc tgaatttta gttttaaaag gatgaaagac ttatgcacag  
 1310 gaagcttcac aacgatataat gtcagatcta aaggtatatt tcaatcgt aattatgta  
 1370 cataaaagca atgtaatca gataaatat gttagagacag aataaaatta attatctc  
 1430 ggtccttcnaa ggcacacag aacagatatac agcagataca cttaatatt catagaaaca  
 1490 aaatacctca aaacctgttt ataaccnaag aatcactgaa aagaaagccc ttgcacatt  
 1550 gcttagaaa gtatttttt taataaaaaat catacttaact attagttact atggagttat  
 1610 atgtacaaat ttctatgtaa aggtcattct tctgtgtag tagaaaaata tgccttact  
 1670 aagttgaaat gaatacttc tgccttgcct catgatagtt atcttaacaa ctcacaaaga  
 1730 aaatatatac ttctatccgg aatatattgt ttgaagcaaa taatataaaac tgtgttgc  
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 Met Lys Phe Val Pro Cys Leu Leu Val Thr Leu Ser Cys Leu  
 15 10 5  
 154 ggg act ttg ggt cag gcc ccg agy caa aag caa gga agc act ggg gag  
 Gly Thr Leu Gly Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Gln  
 20 25 30  
 202 gaa ttc cat ttc cag act gga ggg aga gat tcc tgc act atg cgt ccc  
 Gln Phe His Phe Gln Thr Gly Arg Asp Ser Cys Thr Met Arg Pro  
 35



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	35	40	45	
	agc agc ttg ggg caa ggt gct gga gaa gtc tgg ctt cgc gtc gac tgc	250		
	Ser Ser Leu Gly Gln Gly Ala Gly Glu Val Trp Leu Arg Val Asp Cys			
	50	55	60	
5	cgc aac aca gac cag acc tac tgg tgt gag tac agg ggg cag ccc agc	298		
	Arg Asn Thr Asp Gln Thr Tyr Trp Cys Glu Tyr Arg Gly Gln Pro Ser			
	65	70	75	
	atg tgc cag gct ttc gct gct gac ccc aaa tct tac tgg aat caa gcc	346		
	Met Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala			
10	80	85	90	95
	ctg cag gag ctg agg cgc ctt cac cat gcg tgc cag ggg gcc ccg gtg	394		
	Leu Gln Glu Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val			
	100	105	110	
	ctt agg cca tcc gtg tgc agg gag gct gga ccc cag gcc cat atg cag	442		
15	Leu Arg Pro Ser Val Cys Arg Glu Ala Gly Pro Gln Ala His Met Gln			
	115	120	125	
	cag gtg act tcc agc ctc aag ggc agc cca gag ccc aac cag cag cct	490		
	Gln Val Thr Ser Ser Leu Lys Gly Ser Pro Glu Pro Asn Gln Gln Pro			
	130	135	140	
20	gag gct ggg acg cca tct ctg agg ccc aag gcc aca gtg aaa ctc aca	538		
	Glu Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr			
	145	150	155	
	gaa gca aca cag ctg gga aag gac tcg atg gaa gag ctg gga aaa gcc	586		
	Glu Ala Thr Gln Leu Gly Lys Asp Ser Met Glu Glu Leu Gly Lys Ala			
25	160	165	170	175
	aaa ccc acc acc cga ccc aca gcc aaa cct acc cag cct gga ccc agg	634		
	Lys Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg			
	180	185	190	
	ccc gga ggg aat gag gaa gca aag aag aag gcc tgg gaa cat tgt tgg	682		
30	Pro Gly Gly Asn Glu Glu Ala Lys Lys Lys Ala Trp Glu His Cys Trp			
	195	200	205	
	aaa ccc ttc cag gcc ctg tgc gcc ttt ctc atc agc ttc ttc cga ggg	730		
	Lys Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly			
	210	215	220	
35	tgacaggtga aagacccta cagatctgac ctctccctga cagacaacca tctcttttta	790		

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850 tatatagccg cttccatcc aacgttccca cactggagga agagagtttc taatcaagatg  
 910 caacggccca aattcctgat ctgcagcttc tctgaagttt ggaagagaaa cttccttc  
 970 tggagtttc agagttcagc aatatgatat ggaacaggtg ctgattgggc caagagtgac  
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 102 ctg ctc cta gtc ggc ggc tct ggc atg gtc cgg agc gag gcc tgc  
 Leu Leu Leu Val Ala Ser Ala Met Val Arg Ser Gln Ala Ser  
 5 10 15 20  
 gcc aat ctg ggc gcc gtc gcc agc aag aga tta aag atg cag tac gcc  
 150 Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala  
 25 30 35  
 aag ggg ccg ctg ctc aag ttc aag atc tgt gtc tcc tgaag  
 190 Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser

40  
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 550 agataaactt aatatgattca cctgtgtgtg cttaagctgga atctgttcac ctcccatcca  
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	agtacagacc agatgctttc ttggcaggct cgttgtagct cttggaaaac ctcaatgcaa	790
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	tgaatatttg ttttttatag tttaaaattg atcctttggg aatccagttg aagttcccaa	1090
	atactttata agagtttata agacatctct aatttgacca tgtccagttt atacagttta	1150
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	Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val Thr Gly	
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30	tcc atc aac acg ctc tcg gca aaa tgg gcg gac aat ttc atg gcc gag	152
	Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met Ala Glu	
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	ggc tgt gga ggg agc aag gag cac agc ttc cag cat ccc ttc ctc cag	200
	Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe Leu Gln	
35	35 40 45 50	

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296	ctc ctc cga tgc aga gct gca ggg caa tca gac tcc agc gta gac ccc	65	Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Val Asp Pro	70
		80		75
344	caq caq ccc ttc aac cct ctt ttc ctg ccc cca gcg ctc tgt gac		Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Ala Leu Cys Asp	90
392	atg aca ggg acc agc ctc atg tat gtg gct ctg aac atg acc agt gcc	95	Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr Ser Ala	100
		105		110
440	tcc agc ttc caq atg ctg cgg ggt gca gtg atc ata ttc act ggc ctg		Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Phe Thr Gly Leu	120
		125		130
488	ttc tcc gtg ggc ttc ctg ggc cgg agg ctg gtg ctg agc caq tgg ctg		Phe Ser Val Ala Phe Leu Gly Arg Leu Val Leu Ser Gln Trp Leu	140
		145		150
536	ggc atc cta gcc acc atc gcc ggg ctg gtg gtc gtg ggc ctg gct gac		Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Val Gly Leu Ala Asp	155
		160		170
584	ctc ctg agc aag cac gac agt caq cac aag ctg agc gaa gtg atc aca		Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Gln Val Ile Thr	175
		180		185
632	ggg gac ctg atg atc atg ggc caq atc atc gtt gcc atc caq atg		Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile Gln Met	190
		195		200
680	gtg cta gag gag aag ttc gtc tac aaa caa aat gtg cac cca ctg cgg		Val Leu Gln Gln Lys Phe Val Tyr Lys His Asn Val His Pro Leu Arg	205
		210		220
728	gca gtc ggc act gag ggc ctc ttc ggc ttc gtg atc ctc tcc ctg ctg		Ala Val Gly Thr Gln Gly Leu Phe Gly Phe Val Ile Leu Ser Leu Leu	225
		225		230
776	ctg gtc ccc atg tac tac atc ccc gcc ggc ttc agc gga aac cct		Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly Asn Pro	235
		240		245

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	230	235	240	
	cgt ggg aca ctg gag gat gca ttg gac gcc ttc tgc cag gtg ggc cag			824
	Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val Gly Gln			
	245	250	255	
5	cag ccg ctc att gcc gtg gca ctg ctg ggc aac atc agc agc att gcc			872
	Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser Ile Ala			
	260	265	270	
	ttc ttc aac ttc gca ggc atc agc gtc acc aag gaa ctg agc gcc acc			920
	Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser Ala Thr			
10	275	280	285	290
	acc cgc atg gtg ttg gac agc ttg cgc acc gtt gtc atc tgg gca ctg			968
	Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp Ala Leu			
	295	300	305	
	agc ctg gca ctg ggc tgg gag gcc ttc cat gca ctg cag atc ctt ggc			1016
15	Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile Leu Gly			
	310	315	320	
	ttc ctc ata ctc ctt ata ggc act gcc ctc tac aat ggg cta cac cgt			1064
	Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu His Arg			
	325	330	335	
20	ccg ctg ctg ggc cgc ctg tcc agg ggc cgg ccc ctg gca gag gag agc			1112
	Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu Glu Ser			
	340	345	350	
	gag cag gag aga ctg ctg ggt ggc acc cgc act ccc atc aat gat gcc			1160
	Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn Asp Ala			
25	355	360	365	370
	agc tgagggtccc tggaggettc tactgccacc cgggtgctcc ttotccc			1210
	Ser			
	tgagactgag gccacacagg ctggtgggcc ccgaatgccc tatccccaag gectcaccct			1270
30	gtcccctccc tgcagaaccc ccagggcagc tgctgccaca gaagataaca acacccaagt			1330
	cctctttttc tcaactaccac ctgcagggtg gtgttaccca gccccacaa gectgagtgc			1390
	agtggcagac ctcagctctc tggaccctc ctacagcact agagctaaat catgaagttg			1450
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20 40 45 50  
246 55 60 65  
25 70 75 80 85  
340 gct acc atc cgc atg tgaagtggaaa gatgggctct gtgtgcccgc g  
Ala thr ile arg met  
90

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400 atgaaagactg agctctcttcc cagctcactgc ccagggtggaaa tcaatgctgaaa tgaagacaaggc  
460 cagggttacc agcgcttctc cctctacaat cgcctcacac atccctccgaa aaagtgtgtg  
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	tggtgttctgc ccaccccggg ccgcgtgagt gggggcccaac gcagctcccc gcactccgtg	180
15	ggccaaacttg gccaaagcaac tctgtccggg gagcgggtgt tgcgggggggt gagtaccggg	240
	caactgcgcac gcggagctcc aaattcaaac agctgttttc agaggctgga gggcggggcg	300
	actggtagca gctgggggcta ggagaggctt tctctaggag gcggccgctc gggagcc	357
20	atg gtg gac cgg ggc cct ctg etc acc tcg gcc atc atc ttc tac ctg	405
	Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu	
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	gcc atc ggg gcg gcg atc ttc gaa gtg ctg gag gag cca cac tgg aag	453
	Ala Ile Gly Ala Ala Ile Phe Glu Val Leu Glu Glu Pro His Trp Lys	
25	20 25 30	
	gag gcc aag aaa aac tac tac aca cag aag ctg cat ctg etc aag gag	501
	Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu	
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	ttc ccg tgc ctg ggt cag gag gcc ctg gac aag atc cta gag gtg gta	549
30	Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val	
	50 55 60	
	tct gat gct gca gga cag ggt gtg gcc atc aca ggg aac cag acc ttc	597
	Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe	
	65 70 75 80	
35	aac aac tgg aac tgg ccc aat gca atg att ttt gca gcg acc gtc att	645

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	Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile	85	90	95	
693	acc acc att gga tat ggc nat gtc gct ccc aag acc ccc gcc ggt cgc				
	Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg	100	105	110	
741	ctc ttc tgt gtt ttc tat ggt ctc ttc ggg gtc cgc tgc ctg acg				
	Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr	115	120	125	
789	tgg atc agt gcc ctg ggc aag ttc ttc ggg gga cgt gcc aag aga cta				
	Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Arg Ala Lys Arg Leu	130	135	140	
	ggg cag ttc ctt acc aag aga ggt gtc agt ctg cgg aag gcc cag atc				
837	Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile	145	150	155	160
	acg tgc aca gtc atc ttc atc gtc tgg ggc gtc cta gtc cac ctg gtc				
885	Thr Cys Thr Val Ile Phe Ile Val Trp Gly Val Leu Val His Leu Val	165	170	175	
	atc cca ccc ttc gta ttc atg gtc act gag ggg tgg aac tac atc gag				
933	Ile Pro Pro Phe Val Phe Met Val Thr Gln Gly Trp Asn Tyr Ile Gln	180	185	190	
	ggc ctc tac tac ttc atc acc atc tcc acc atc ggc ttc ggt gac				
981	Gly Leu Tyr Tyr Ser Phe Ile Thr Ile Ser Thr Ile Gly Phe Gly Asp	195	200	205	
	ttt gtc gcc ggt gtc aac ccc acc gcc aac tac cac gcc ctg tac cgc				
1029	Phe Val Ala Gly Val Asn Pro Ser Ala Asn Tyr His Ala Leu Tyr Arg	210	215	220	
	tac ttc gtc gag ctc tgg atc tac tgc ggg ctg gcc tgg ctg tcc ctc				
1077	Tyr Phe Val Gln Leu Trp Ile Tyr Leu Gly Leu Ala Trp Leu Ser Leu	225	230	235	240
	ttt gtc aac tgg aag gtc agc atg ttt gtc gaa gtc cac aaa gcc att				
1125	Phe Val Asn Trp Lys Val Ser Met Phe Val Gln Val His Lys Ala Ile	245	250	255	
	aag aag cgg cgg cga cgg aag gag tcc ttt gag agc tcc cca cac				
1173	Lys Lys Arg Arg Arg Arg Arg Arg Arg Arg Arg Arg Arg Arg Arg	260	265	270	
35					
30					
25					
20					
15					
10					
5					



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	Ser Arg Lys Ala Leu Gln Val Lys Gly Ser Thr Ala Ser Lys Asp Val	
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	aac atc ttc agc ttt ctt tcc aag aag gaa gag acc tac aac gac ctc	1269
5	Asn Ile Phe Ser Phe Leu Ser Lys Lys Glu Glu Thr Tyr Asn Asp Leu	
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	atc aag cag atc ggg aag aag gcc atg aag aca agc ggg ggt ggg gag	1317
	Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu	
	305 310 315 320	
10	acg ggc ccg ggc cca ggg ctg ggg cct caa ggc ggt ggg ctc cca gca	1365
	Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Gly Leu Pro Ala	
	325 330 335	
	ctg ccc cct tcc ctg gtg ccc ctg gta gtc tac tcc aag aac cgg gtg	1413
	Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val	
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	ccc acc ttg gaa gag gtg tca cag aca ctg agg agc aaa ggc cac gta	1461
	Pro Thr Leu Glu Glu Val Ser Gln Thr Leu Arg Ser Lys Gly His Val	
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	tca agg tcc cca gat gag gag gct gtg gca cgg gcc cct gaa gac agc	1509
20	Ser Arg Ser Pro Asp Glu Glu Ala Val Ala Arg Ala Pro Glu Asp Ser	
	370 375 380	
	tcc cct gcc ccc gag gtg ttc atg aac cag ctg gac cgc atc agc gag	1557
	Ser Pro Ala Pro Glu Val Phe Met Asn Gln Leu Asp Arg Ile Ser Glu	
	385 390 395 400	
25	gaa tgc gag cca tgg gac gcc cag gac tac cac cca ctc atc ttc cag	1605
	Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln	
	405 410 415	
	gac gcc agc atc acc ttc gtg aac acg gag gct ggc ctc tca gac gag	1653
	Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu	
30	420 425 430	
	gag acc tcc aag tcc tcg cta gag gac aac ttg gca ggg gag gag agc	1701
	Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser	
	435 440 445	
	ccc cag cag ggg gct gaa gcc aag gcg ccc ctg aac atg ggc gag ttc	1749
35	Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe	

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450	455	460	1797	Pro Ser Ser Glu Ser Thr Phe Thr Glu Ser Leu Ser ccc tcc tcc tcc gag tcc acc ttc acc agc act gag tct gag ctc tct
465	470	475	1845	Val Pro Tyr Glu Glu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro gtg cct tac gaa cag ctg atg tat gag tac aac aag gct aac agc ccc
485	490	495	1890	asn ggc aca tgaagcaagg ccggctcccc accccaacct tgaatgg Lys Gly Thr

10

15

20

25

30

35

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	gat tct aag cgt gga gag gcc ccg ttc gct cag cgt atc gac ccg act	101
	Asp Ser Lys Arg Gly Glu Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr	
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	cgg gag aag ctg aca ccc gag caa ctg cat tcc atg cgg cag gcg gag	149
25	Arg Glu Lys Leu Thr Pro Glu Gln Leu His Ser Met Arg Gln Ala Glu	
	30 35 40	
	ott gcc cag tgg cag aag gtc cta cca cgg cgg cga acc cgg aac atc	197
	Leu Ala Gln Trp Gln Lys Val Leu Pro Arg Arg Arg Thr Arg Asn Ile	
	45 50 55	
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	Val Thr Gly Leu Gly Ile Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr	
	60 65 70	
	acc ttc tac tcg att tcc cag gag cgt ttc cta gat gag cta gaa gac	293
	Thr Phe Tyr Ser Ile Ser Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp	
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 341 gln ala lys ala arg ala arg ala leu ala arg ala ser gly ser  
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 1  
 5  
 gct tac aac aac ata acc ggc agg caa gat gaa act cat ttc aca gtt  
 161 ala tyr asn asn ile thr gly arg gln asp gln thr his phe thr val  
 10 15 20  
 atc atc acc tcc gta gga ctg gag aag ctt gca cag aaa gga aaa tca  
 209 ile ile thr ser val gly leu gln lys leu ala gln lys gly lys ser  
 25 30 35  
 ttg tca cct tta gca agt ata act gga ata tca cta ttt ttg att ata  
 257 leu ser pro leu ala ser ile thr gly ile ser leu phe leu ile ile  
 40 45 50  
 tcc atg tgt ctt ctc ttc cta tgg aaa aaa tat caa ccc tac aaa gtt  
 305

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Ser Met Cys Leu Leu Phe Leu Trp Lys Lys Tyr Gln Pro Tyr Lys Val  
 55 60 65 70  
 ata aaa cag aaa cta gaa ggc agg cca gaa aca gaa tac agg aaa gct 353  
 Ile Lys Gln Lys Leu Glu Gly Arg Pro Glu Thr Glu Tyr Arg Lys Ala  
 5 75 80 85  
 caa aca ttt tca ggc cat gaa gat gct ctg gat gac ttc gga ata tat 401  
 Gln Thr Phe Ser Gly His Glu Asp Ala Leu Asp Asp Phe Gly Ile Tyr  
 90 95 100  
 gaa ttt gtt gct ttt cca gat gtt tct ggt gtt tcc agg atc cca agc 449  
 10 Glu Phe Val Ala Phe Pro Asp Val Ser Gly Val Ser Arg Ile Pro Ser  
 105 110 115  
 agg tct gtt cca gcc tct gat tgt gta tcc ggg caa gat ttg cac agt 497  
 Arg Ser Val Pro Ala Ser Asp Cys Val Ser Gly Gln Asp Leu His Ser  
 120 125 130  
 15 aca gtg tat gaa gtt att cag cac atc cct gcc cag cag caa gac cat 545  
 Thr Val Tyr Glu Val Ile Gln His Ile Pro Ala Gln Gln Gln Asp His  
 135 140 145 150  
 cca gag tgaactttca tgggctaaac agtacattcg agtgaaattc tgaagaac 600  
 Pro Glu  
 20  
 attttaagga aaaacagtgg aaaagtatat taatctggaa tcagtgaaga aaccaagacc 660  
 aacacctctt actcattatt cctttacatg cagaatagag gcatttatgc aaattgaact 720  
 gcaggttttt cagcatatac acaatgtctt gtgcaacaga aaaacatggt ggggaaatat 780  
 tcctcagtgg agagtcgttc tcatgctgac ggggagaacg aaagtgacag gggtttcctc 840  
 25 ataagttttg tatgaaatat ctotacaaac ctcaattagt tctactctac actttcacta 900  
 tcatcaacac tgagactatc ctgtctcacc taaaaatgtg gaaactttac attgttcgat 960  
 ttttcagcag actttgtttt attaaatttt tattagtgtt aagaatgcta aagtttcaat 1020  
 tttatttcca aatttctatc ttgttatttg tacaacaaag taataaggat ggttgcaca 1080  
 aaaacaaaac tatgccttct cttttttttc aatcaccagt agtatttttg agaagacttg 1140  
 30 tgaacactta aggaaatgac tattaaagtc ttatttttat ttttttcaag gaaagatgga 1200  
 ttcaataaaa ttattctggt tttgctttt 1229

&lt;210&gt; 91

&lt;211&gt; 358

35 &lt;212&gt; PRT

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<213> Homo sapiens

<400> 91

Met Ala Pro Gln Asn Leu Ser Thr Phe Cys Leu Leu Leu Tyr Leu  
1 5 10 15

Ile Gly Ala Val Ile Ala Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val  
20 25 30

Pro Arg Ser Ala Ser Ile Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu  
35 40 45

Ala Leu Gln Leu His Pro Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln  
50 55 60

Gln Lys Phe Gln Asp Leu Gly Ala Tyr Gln Val Leu Ser Asp Ser  
65 70 75 80

Gln Lys Arg Lys Gln Tyr Asp Thr Tyr Gly Gln Gly Leu Lys Asp  
85 90 95

Gly His Gln Ser Ser His Gly Asp Ile Phe Ser His Phe Phe Gly Asp  
100 105 110

Phe Gly Phe Met Phe Gly Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile  
115 120 125

Pro Arg Gly Ser Asp Ile Ile Val Asp Leu Gln Val Thr Leu Gln Gln  
130 135 140

Val Tyr Ala Gly Asn Phe Val Gln Val Val Arg Asn Lys Pro Val Ala  
145 150 155 160

Arg Gln Ala Pro Gly Lys Arg Lys Cys Asn Cys Arg Gln Gln Met Arg  
165 170 175

Thr Thr Gln Leu Gly Pro Gly Arg Phe Gln Met Thr Gln Gln Val Val  
180 185 190

Cys Asp Gln Cys Pro Asn Val Lys Leu Val Asn Gln Arg Thr Leu  
195 200 205

Gln Val Gln Ile Gln Pro Gly Val Arg Asp Gly Met Gln Tyr Pro Phe  
210 215 220

Ile Gly Gln Gly Gln Pro His Val Asp Gly Gln Pro Gly Asp Leu Arg  
225 230 235 240

Phe Arg Ile Lys Val Val Lys His Pro Ile Phe Gln Arg Arg Gly Asp  
245 250 255

35

30

25

20

15

10

5

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Asp Leu Tyr Thr Asn Val Thr Ile Ser Leu Val Glu Ser Leu Val Gly  
                   260                  265                  270  
 Phe Glu Met Asp Ile Thr His Leu Asp Gly His Lys Val His Ile Ser  
                   275                  280                  285  
 5 Arg Asp Lys Ile Thr Arg Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu  
                   290                  295                  300  
 Gly Leu Pro Asn Phe Asp Asn Asn Asn Ile Lys Gly Ser Leu Ile Ile  
 305                  310                  315                  320  
 Thr Phe Asp Val Asp Phe Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg  
 10                  325                  330                  335  
 Glu Gly Ile Lys Gln Leu Leu Lys Gln Gly Ser Val Gln Lys Val Tyr  
                   340                  345                  350  
 Asn Gly Leu Gln Gly Tyr  
                   355  
 15  
 <210> 92  
 <211> 226  
 <212> PRT  
 <213> Homo sapience  
 20  
 <400> 92  
 Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser Asn Ser Cys Cys  
   1                  5                  10                  15  
 Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu Gly Val Trp Tyr  
 25                  20                  25                  30  
 Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu Ser Ala Leu Ala  
                   35                  40                  45  
 Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu Gly Gly Asp Phe  
                   50                  55                  60  
 30 Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile Ala Ile Ser Leu  
                   65                  70                  75                  80  
 Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly Ala Tyr Lys Gln  
                   85                  90                  95  
 Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln Ile Phe Asp Phe  
 35                  100                  105                  110

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35	85	90	95
30	50	55	60
25	1	5	10
20	<210> 93	<211> 195	<212> PRT
15	225	210	215
10	180	185	190
5	145	150	155
	130	135	140
	115	120	125
	165	170	175
	195	200	205
	210	215	220
	225		
	<210> 93	<211> 195	<212> PRT
	<213> Homo sapiens		
	<400> 93		



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Ile Gly Leu Ile Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met  
                   100                  105                  110  
 Gln Ala Pro Ser Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala  
                   115                  120                  125  
 5 Cys Met Met Val Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met  
                   130                  135                  140  
 Ser Thr Gly Ala Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser  
                   145                  150                  155                  160  
 Lys Leu Glu Ser Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile  
 10                                   165                  170                  175  
 Leu Asp Asn Glu Met Lys Leu Asn Val His Met Asp Ser Ile Pro His  
                   180                  185                  190  
 His Arg Ser  
                   195  
 15  
 <210> 94  
 <211> 339  
 <212> PRT  
 <213> Homo sapience  
 20  
 <400> 94  
 Met Asn Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu  
                   1                  5                  10                  15  
 Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu  
 25                                   20                  25                  30  
 Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu  
                   35                  40                  45  
 Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu  
                   50                  55                  60  
 30 Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser  
                   65                  70                  75                  80  
 Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu  
                   85                  90                  95  
 Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu  
 35                                   100                  105                  110

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Thr Asp Thr Gly Ser His Glu Ala Thr Lys Ala Val Leu Glu

115 120 125

Phe Gly Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Glu Arg

130 135 140

Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu

145 150 155

Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His

165 170 175

Met Ile Glu Arg Lys Glu Gly Lys Ile Val Thr Val Asn Ser Ile Leu

180 185 190

Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His

195 200 205

Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr

210 215 220

Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Glu Ser Asn

225 230 235

Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn

245 250 255

Asn Gly Asp Glu Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu

260 265 270

Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Thr Ile Ser Glu

275 280 285

Gln Pro Phe Leu Leu Val Thr Tyr Leu Tyr Glu Tyr Met Pro Thr Trp

290 295 300

Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe

305 310 315

Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr

325 330 335

Lys His Asp

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<213> Homo sapiens

<212> PRT

<211> 487

<210> 95

30

25

20

15

10

5

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<400> 95
Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys
  1             5             10             15
Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro
5             20             25             30
Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val
  35             40             45
Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser
  50             55             60
10 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu
  65             70             75             80
Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe
             85             90             95
Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu
15             100             105             110
Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala
  115             120             125
Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser
  130             135             140
20 Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu
  145             150             155             160
Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Glu Glu Val
             165             170             175
Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala
25             180             185             190
Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile
  195             200             205
Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile
  210             215             220
30 Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val
  225             230             235             240
Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu
             245             250             255
Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala
35             260             265             270

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lys gln ser pro ile val lys ile leu lys phe gly trp phe pro	275	280	285
ile ile leu ala met val ile ser ser phe gly gly ile leu ser	290	295	300
lys thr val ser lys gln gln tyr lys gly met ala ile phe thr pro	305	310	315
val ile cys gly val gly gly asn leu val ala ile gln thr ser arg	325	330	335
ile ser thr tyr leu his met trp ser ala pro gly val leu pro leu	340	345	350
gln met lys lys phe trp pro asn pro cys ser thr phe cys thr ser	355	360	365
gln ile asn ser met ser ala arg val leu leu leu val val pro	370	375	380
gly his leu ile phe phe tyr ile ile tyr leu val gln gly gln ser	385	390	395
val ile asn ser gln thr phe val val leu tyr leu leu ala gly leu	405	410	415
ile gln val thr ile leu leu tyr leu ala gln val met val arg leu	420	425	430
thr trp his gln ala leu asp pro asp asn his cys ile pro tyr leu	435	440	445
thr gly leu gly asp leu leu gly thr gly leu leu ala leu cys phe	450	455	460
phe thr asp trp leu leu lys ser lys ala gln leu gly gly ile ser	465	470	475
gln leu ala ser gly pro pro	485		480
<210> 96			
<211> 393			
<212> PRT			
<213> Homo sapiens			
<400> 96			

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Met Arg Thr Leu Phe Asn Leu Leu Trp Leu Ala Leu Ala Cys Ser Pro  
 1 5 10 15  
 Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala Ala Ser Lys  
 20 25 30  
 5 Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp Lys Pro Val Gln Asp Arg  
 35 40 45  
 Gly Leu Val Val Thr Asp Leu Lys Ala Glu Ser Val Val Leu Glu His  
 50 55 60  
 Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp Arg His Phe Ala Gly Asp  
 10 65 70 75 80  
 Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr Asp Val Thr  
 85 90 95  
 Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val Trp Leu Gln  
 100 105 110  
 15 Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Val Thr Gly Leu His Asp  
 115 120 125  
 Val Asp Gln Gly Trp Met Arg Ala Val Arg Lys His Ala Lys Gly Leu  
 130 135 140  
 His Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr Asp Asp Phe  
 20 145 150 155 160  
 Arg Asn Val Leu Asp Ser Glu Asp Glu Ile Glu Glu Leu Ser Lys Thr  
 165 170 175  
 Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe Val Val Glu  
 180 185 190  
 25 Val Trp Asn Gln Leu Leu Ser Gln Lys Arg Val Gly Leu Ile His Met  
 195 200 205  
 Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu Leu Ala Leu  
 210 215 220  
 Leu Val Ile Pro Pro Ala Ile Thr Pro Gly Thr Asp Gln Leu Gly Met  
 30 225 230 235 240  
 Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Val Leu Asp Gly Phe  
 245 250 255  
 Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala His Gln Pro Gly Pro Asn  
 260 265 270  
 35 Ala Pro Leu Ser Trp Val Arg Ala Cys Val Gln Val Leu Asp Pro Lys

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35	gln gln val thr leu gln pro gly gln tyr ile thr lys val phe val	85	90	95
	leu gly asp ser trp asp val lys leu gly ala leu gly gly asn thr	65	70	75
	leu arg val ser val gly leu leu leu val lys ser val gln val lys	50	55	60
30	gly lys tyr phe ser thr thr gln asp tyr asp his gln ile thr gly	35	40	45
	leu leu gly gly pro thr trp ala gly lys met tyr gly pro gly gly	20	25	30
25	pro gly met his arg pro gln ala met leu leu leu thr leu ala	1	5	10
	met trp arg val pro gly thr thr arg arg pro val thr gly gln ser	<210> 97		
20	<210> 97 <211> 196 <212> PRT <213> Homo sapiens			
15	gly leu asp tyr phe tyr asp leu leu	385	390	
	leu ala arg gln leu gly val gly val ser ile trp gln leu gly gln	370	375	380
10	his val val phe tyr pro thr leu lys ser leu gln val arg leu gln	355	360	365
	gln ala ser gln his phe gln tyr lys lys ser arg ser gly arg	340	345	350
5	tyr ile gln thr leu lys asp his arg pro arg met val trp asp ser	325	330	335
	asp tyr ala thr ser lys asp ala arg gln pro val val gly ala arg	305	310	315
	ser lys trp arg ser lys ile leu leu gly leu asn phe tyr gly met	290	295	300
		275	280	285

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100 105 110  
 Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser Lys Asp  
 115 120 125  
 Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser Ala Tyr  
 5 130 135 140  
 Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln Tyr Gln  
 145 150 155 160  
 Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro Leu Glu  
 165 170 175  
 10 Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala Asn Ser  
 180 185 190  
 Pro Val Gly Arg  
 195  
  
 15 <210> 98  
 <211> 107  
 <212> PRT  
 <213> Homo sapience  
  
 20 <400> 98  
 Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met Ser  
 1 5 10 15  
 Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly Ser  
 20 25 30  
 25 Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly Ile  
 35 40 45  
 Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys Ser  
 50 55 60  
 Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val Ala  
 30 65 70 75 80  
 Ala Glu Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr Ser  
 85 90 95  
 Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro  
 100 105  
 35

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<210> 99  
<211> 350  
<212> PRT  
<213> Homo sapiens

5

<400> 99

Met Ser Gln Val Lys Ser Arg Lys Lys Ser Gly Pro Lys Gly Ala Pro  
1 5 10 15

Ala Ala Gln Pro Gly Lys Arg Ser Gln Gly Gly Lys Thr Pro Val Ala  
20 25 30

Arg Ser Ser Gly Gly Gly Gly Trp Ala Asp Pro Arg Thr Cys Leu Ser  
35 40 45

Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala Trp Phe Val Phe Gln  
50 55 60

Gln Ser Gln Lys Phe Ala Lys Val Gln Asn Gln Tyr Gln Leu Lys  
65 70 75 80

Leu Gln Thr Asn Gln Phe Gln Gln Leu Gln Ser Lys Ile Ser Leu Ile  
85 90 95

Ser Gln Lys Trp Gln Lys Ser Gln Ala Ile Met Gln Gln Leu Lys Ser  
100 105 110

Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln Gln Ile Asn Gln  
115 120 125

Val Lys Thr Trp Ser Asn Arg Ile Thr Gln Lys Gln Asp Ile Leu Asn  
130 135 140

Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr Lys Val Asp Gln Ser  
145 150 155 160

Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys Ile Thr Ser Val Lys  
165 170 175

Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr Asp Val Ile Ser Leu  
180 185 190

Thr Asp Ser Val Gln Gln Leu Gln Asn Lys Ile Gln Lys Val Gln Lys  
195 200 205

Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser Ser Ile Asp Arg  
210 215 220

Thr Ala Thr Leu Arg Lys Thr Ala Ser Gln Asn Ser Gln Arg Ile Asn  
220 225 230

35

30

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20

15

10



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225                      230                      235                      240  
 Ser Val Lys Lys Thr Leu Thr Glu Leu Lys Ser Asp Phe Asp Lys His  
                          245                      250                      255  
 Thr Asp Arg Phe Leu Ser Leu Glu Gly Asp Arg Ala Lys Val Leu Lys  
 5                      260                      265                      270  
 Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys Val Tyr Asn Leu Lys  
                          275                      280                      285  
 Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn Asp Leu Thr Leu Arg  
                          290                      295                      300  
 10    Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg Glu Lys Glu Ile Ala  
                          305                      310                      315                      320  
 Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile Val Gln Ala Glu Ile  
                          325                      330                      335  
 Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser Asp Met Asn  
 15                      340                      345                      350  
  
 <210> 100  
 <211> 107  
 <212> PRT  
 20    <213> Homo sapience  
  
 <400> 100  
 Met Ser Ser Ala Gly Thr Ala Thr Pro Leu Glu Met Asp His Lys Leu  
       1                      5                      10                      15  
 25    Thr Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser  
                          20                      25                      30  
 Ile Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Glu  
                          35                      40                      45  
 Ser Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val  
 30                      50                      55                      60  
 Asn Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu  
                          65                      70                      75                      80  
 Leu Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly  
                          85                      90                      95  
 35    Arg Pro Ala Gly Gly Ala His Leu Cys Ala Ala

100

<400> 101

09      ԵՂԵՆԵՆԵՆԻ ՆԱԽԱՆԱԽՆԱԽ    ԵՂԵՆԵՆԵՆԻ ՆԱԽԱՆԱԽՆԱԽ    ԵՂԵՆԵՆԵՆԻ ՆԱԽԱՆԱԽՆԱԽ    ԵՂԵՆԵՆԵՆԻ ՆԱԽԱՆԱԽՆԱԽ    ԵՂԵՆԵՆԵՆԻ ՆԱԽԱՆԱԽՆԱԽ

<400> 101

[illegible][illegible]

<210> 102  
<211> 678  
<212> DNA  
<213> Homo Sapiens

<400> 102

[illegible]

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 ggaggtgact ttgagttoat ggatgatgcc aacatgtgca ttgccattgc gattttctctt 240  
 ctcattgatcc tgatatgtgc tatggctact tacggagcgt acaagcaacg cgcagcctgg 300  
 atcatcccat tcttctgtta ccagatcttt gactttgccc tgaacatggt gggtgcaatc 360  
 5 actgtgctta tttatccaaa ctccattcag gaatacatat gccaaactgcc tcttaatttt 420  
 ccctacagag atgatgtcat gtcagtgaat cctacctgtt tggctcttat tattctcttg 480  
 tttattagca ttatcttgac ttttaagggt tacttgatta gctgtgtttg gaactgctac 540  
 cgatacatca atggtaggaa ctctctgat gtcctgggtt atgttaccag caatgacact 600  
 acgggtgctgc taccctcgta tgatgatgcc actgtgaatg gtgctgccc aaaggccaccg 660  
 10 ccaccttaacg tgtctgcc 678

&lt;210&gt; 103

&lt;211&gt; 585

&lt;212&gt; DNA

15 &lt;213&gt; Homo Sapience

&lt;400&gt; 103

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 gccaatctgg gggcggtgcc cagcaagaga ttaaagatgc agtacgccac ggggccgctg 120  
 20 ctcaagttcc agatttgtgt ttcttgaggt tataggcggt tgtttgagga gtacatggcg 180  
 gttattagcc agcggtagcc agacatccgc attgaaggag agaattacct ccctcaacca 240  
 atatatagac acatagcatc ttctctgtca gtcttcaaac tagtattaat aggettaata 300  
 attgttggca aggatccttt tgctttcttt ggcattgcaag ctctagcat ctggcagtg 360  
 ggccaagaaa ataaggttta tgcattgtat atggttttct tcttgagcaa catgattgag 420  
 25 aaccagtgtg tgtcaacagg tgcatttgag ataacttta atgatgtacc tgtgtgtct 480  
 aagctggaat ctggtcacct tccatccatg caacaacttg ttcaaattct tgacaatgaa 540  
 atgaagctca atgtgcatat ggattcaatc ccacaccatc gatca 585

&lt;210&gt; 104

30 &lt;211&gt; 1017

&lt;212&gt; DNA

&lt;213&gt; Homo Sapience

&lt;400&gt; 104

35 atgaactggg agctgctgct gtggtgctg gtgctgtgag cgtgctcct gctcttggtg 60

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5	120	caugetcgtc gctccctcag ggcctcagac gaccctcagac taccatcggc cgaatcggcag
	180	ggagagagagc cagaaatggga gctgacatgat atggtcgggt gggtgacatgg agcctcggat
	240	ggaaatcgggt agagacatgg taccacagctg taccacagctg gactctcctc tgtcgtcgtc
	300	ggcagagagag tgcacatggat ggcagagagat ggcagagagat ggcagagagat tggcagatc
	360	aaagaaagag ataatcctgt tctgcgcctt gacccctgacg acaatcgttc ccatggagc
10	420	gctaacaaag cgtctcctca ggaatcctgt agaatcggca tctcgtgctca caatgggtgga
	480	atgtcccaag gctcctcgtg catggatcac agctcgtgatg tctacagga gctaatagag
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	600	aaagcaggaag agatcgttac tgtgaatagc atccctgggt tcaatcctgt accctctc
	660	atcggatcac gctcctagca gcaatcgtcc cgggtgtctt ttaatggcct tcgaaacagga
	720	ctcgcacacac acccaggtat aatagcttcc aaatccttc caggacccgt gcaatcaca
	780	atcgtggagaa atccctcagc tcgagagatc acaagacata taggcataa tcgagagacag
	840	tcacacagaa tgaacacag tgcgtcgtgt cggctcgtat taatcagcat ggcacatgat
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	960	atgcacacac atgcctcgtg gatcacacac aaatcggggga agaaagagat tgaagaaatc
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	240	accgctcgtc ccaatcagcctc tcaggtcgaac gtcgccccctc tgtctcgtcag cctcggagcctg
	300	tcctcgggccc gcaatcgtctc ggaatattc cagacatcggc ctcgtgtctc ggaatcga
	360	gaacctcttga caatcgtgtc ggcctcgggt ggcctcggag ggaacccctgga gactgacac
	420	gcacccagaa tctcccaagc atcgagctca ttcgtgctca ggaatcggca ttcgtgctgga
	480	atgtcccaag gctcctcgtg catggatcac agctcgtgatg tctacagga gctaatagag
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	600	aaagcaggaag agatcgttac tgtgaatagc atccctgggt tcaatcctgt accctctc
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	720	ctcgcacacac acccaggtat aatagcttcc aaatccttc caggacccgt gcaatcaca
	780	atcgtggagaa atccctcagc tcgagagatc acaagacata taggcataa tcgagagacag
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	660	atcggatcac gctcctagca gcaatcgtcc cgggtgtctt ttaatggcct tcgaaacagga
	720	ctcgcacacac acccaggtat aatagcttcc aaatccttc caggacccgt gcaatcaca
	780	atcgtggagaa atccctcagc tcgagagatc acaagacata taggcataa tcgagagacag
	840	tcacacagaa tgaacacag tgcgtcgtgt cggctcgtat taatcagcat ggcacatgat
	900	ctgaagagag tctggtatcc agaacacac tctcctgtcag taacatattc gctggcaatac
	960	atgcacacac atgcctcgtg gatcacacac aaatcggggga agaaagagat tgaagaaatc
	1017	aaagatcgtg tcgacatcag cctctctat ttcaaaatcc tcagagacaa acatgac

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	atcctgaagt ttggctggtt cccaatcctc ctggccatgg tcatcagcag ttccggagga	900
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	tcagataagc cgggtgcaaga ccgggggttg gtggtgacgg acctcaaagc tgagagtgtg	180
	gttcttgagc atgcagcta ctgctcggca aaggcccggt acagacactt tgcctgggat	240
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	aagcggtgg gcctcatcca catgctcacc cacttgccg aggtcttga ccaggcccg	660
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	ttcacgcaca aggagtttga gcagctggcc cccgtgctgg atggtttcag cctcatgacc	780
	tacgactact ctacagcga tcagcctggc cctaatac cctgtcctg ggttcgagcc	840
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<400> 108

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&lt;211&gt; 1050

&lt;212&gt; DNA

5 &lt;213&gt; Homo Sapience

&lt;400&gt; 109

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	gggaagcggg gcgagggcgg gaagaccccc gtggcccgga gcagcggagg cgggggctgg	120
10	gcagaccccc gaacgtgcct gagcctgctg tcgctgggga cgtgcctggg cctggcctgg	180
	tttgtatttc agcagtcaga aaaatttgca aaggtggaaa accaatacca gttactgaaa	240
	ctagaaacca atgaattcca acaacttcaa agtaaaatca gtttaatttc agaaaagtgg	300
	cagaaatctg aagctatcat ggaacaattg aagtcttttc aaataattgc tcatctaaag	360
	cgtctacagg aagaaattaa tgaggtaaaa acttggtcca ataggataac tgaaaaacag	420
15	gatatactga acaacagtct gacgacgctt tctcaagaca ttacaaaagt agaccaaagt	480
	acaacttcca tggcaaaaga tgttggtctc aagattacaa gtgtaaaaac agatatacga	540
	cggatttcag gtttagtaac tgatgtaata tcattgacag attctgtgca agaactagaa	600
	aataaaatag agaaagtaga aaaaaataca gtaaaaaata taggtgatct tctttcaagc	660
	agtattgatc gaacagcaac gctccgaaag acagcatctg aaaattcaca aagaattaac	720
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	ctaagcttag aaggtgacag agccaaagtt ctgaagacag tgacttttgc aaatgatcta	840
	aaaccaaagg tgtataatct aaagaaggac ttttccggt tagaaccatt agtaaagat	900
	ttaacactac gcattgggag attggttacc gacttactac aaagagagaa agaaattgct	960
	ttcttaagtg aaaaaatata taatttaaca atagtccaag ctgagattaa ggatattaaa	1020
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&lt;210&gt; 110

&lt;211&gt; 321

&lt;212&gt; DNA

30 &lt;213&gt; Homo Sapience

&lt;400&gt; 110

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	ggcaggccaa gcttctattg taacagtagg cacagtatag tcggatcatt acatcagctg	120
35	ggtttttggg ttagtcatct agagtcgtct ggactaaagg tctttcaggt ctctctgccc	180

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240 tgtgagtgctg tgaacctccc caaccgaatt gctcagattg tccagagcct catgtctctc  
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5

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175 gaggaagtgt tggaaagga cccgggacag aggaacc atg gct ccg cag aac ctg  
Met Ala Pro Gln Asn Leu  
1 I  
5

20

agc acc ttt tgc ctg ttg ctg cta tac ctc atc ggg gcg gctg att gcc  
Ser Thr Phe Cys Leu Leu Leu Tyr Leu Ile Gly Ala Val Ile Ala  
10 15 20  
gga cga gat ttc tat aag atc ttg ggg gctg cct cga agt gcc tct ata  
271 Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val Pro Arg Ser Ala Ser Ile  
25 30 35  
aag gat att aaa aag gcc tat agg aaa cta gcc ctg cag ctt cat ccc  
319 Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu Ala Leu Gln Leu His Pro  
40 45 50  
gac cgg aac cct gat gat cca caa gcc cag gag aaa ttc cag gat ctg  
367 Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln Lys Phe Gln Asp Leu  
55 60 65 70  
ggt gct gct tat gag gtt ctg tca gat agt gag aaa cgg aaa cag tac  
415 Gly Ala Ala Tyr Gln Val Leu Ser Asp Ser Gln Lys Arg Lys Gln Tyr  
75 80 85  
gat act tat ggt gaa gaa gga tca aaa gat ggt cat cag agc tcc cat  
463 Asp Thr Tyr Gly Gln Gln Gly Leu Lys Asp Gly His Gln Ser Ser His

25

30

35



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	gga gac att ttt tca cac ttc ttt ggg gat ttt ggt ttc atg ttt gga	511		
	Gly Asp Ile Phe Ser His Phe Phe Gly Asp Phe Gly Phe Met Phe Gly			
	105	110	115	
5	gga acc cct cgt cag caa gac aga aat att cca aga gga agt gat att	559		
	Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile Pro Arg Gly Ser Asp Ile			
	120	125	130	
	att gta gat cta gaa gtc act ttg gaa gaa gta tat gca gga aat ttt	607		
	Ile Val Asp Leu Glu Val Thr Leu Glu Glu Val Tyr Ala Gly Asn Phe			
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	gtg gaa gta gtt aga aac aaa cct gtg gca agg cag gct cct ggc aaa	655		
	Val Glu Val Val Arg Asn Lys Pro Val Ala Arg Gln Ala Pro Gly Lys			
	155	160	165	
	cgg aag tgc aat tgt cgg caa gag atg cgg acc acc cag ctg ggc cct	703		
15	Arg Lys Cys Asn Cys Arg Gln Glu Met Arg Thr Thr Gln Leu Gly Pro			
	170	175	180	
	ggg cgc ttc caa atg acc cag gag gtg gtc tgc gac gaa tgc cct aat	751		
	Gly Arg Phe Gln Met Thr Gln Glu Val Val Cys Asp Glu Cys Pro Asn			
	185	190	195	
20	gtc aaa cta gtg aat gaa gaa cga acg ctg gaa gta gaa ata gag cct	799		
	Val Lys Leu Val Asn Glu Glu Arg Thr Leu Glu Val Glu Ile Glu Pro			
	200	205	210	
	ggg gtg aga gac ggc atg gag tac ccc ttt att gga gaa ggt gag cct	847		
	Gly Val Arg Asp Gly Met Glu Tyr Pro Phe Ile Gly Glu Gly Glu Pro			
25	215	220	225	230
	cac gtg gat ggg gag cct gga gat tta cgg ttc cga atc aaa gtt gtc	895		
	His Val Asp Gly Glu Pro Gly Asp Leu Arg Phe Arg Ile Lys Val Val			
	235	240	245	
	aag cac cca ata ttt gaa agg aga gga gat gat ttg tac aca aat gtg	943		
30	Lys His Pro Ile Phe Glu Arg Arg Gly Asp Asp Leu Tyr Thr Asn Val			
	250	255	260	
	aca atc tca tta gtt gag tca ctg gtt ggc ttt gag atg gat att act	991		
	Thr Ile Ser Leu Val Glu Ser Leu Val Gly Phe Glu Met Asp Ile Thr			
	265	270	275	
35	cac ttg gat ggt cac aag gta cat att tcc cgg gat aag atc acc agg	1039		

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15	345 350 355 Leu Lys Glu Ser Val Glu Lys Val Tyr Asn Gly Leu Glu Gly Tyr ctg aaa caa ggg tca gtc cag aag gta tac aat gga ctg caa gga tat	1231
10	330 335 340 Pro Lys Glu Glu Thr Glu Glu Ala Arg Glu Gly Ile Lys Glu Leu cca aaa gaa cag tta aca gag gaa ggc aga gaa ggt atc aaa cag cta	1183
5	315 320 325 Asn Asn Asn Ile Lys Gly Ser Leu Ile Thr Phe Asp Val Asp Phe aac aac aat atc aag ggc tct ttg ata atc act ttt gat gtc gat ttt Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu Gly Leu Pro Asn Phe Asp cca gga ggc aag cta tgg aag aaa ggg gaa ggc ctc ccc aac ttt gac	1087 295 300 305 310
	280 285 290 His Leu Asp Gly His Lys Val His Ile Ser Arg Asp Lys Ile Thr Arg	

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	Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser	
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	aac agc tgc tgc ttg tgc tgc cat gtc cgc acc ggc acc atc ctg ctc	337
5	Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu	
	15 20 25	
	ggc gtc tgg tat ctg atc atc aat gct gtg gta ctg ttg att tta ttg	385
	Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu	
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10	agt gcc ctg gct gat ccg gat cag tat aac ttt tca agt tct gaa ctg	433
	Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu	
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	Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile	
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	Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly	
	80 85 90	
	gcg tac aag caa cgc gca gcc tgg atc atc cca ttc ttc tgt tac cag	577
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	95 100 105	
	atc ttt gac ttt gcc ctg aac atg ttg gtt gca atc act gtg ctt att	625
	Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile	
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	Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe	
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	ccc tac aga gat gat gtc atg tca gtg aat cct acc tgt ttg gtc ctt	721
	Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu	
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	att att ctt ctg ttt att agc att atc ttg act ttt aag ggt tac ttg	769
	Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu	
	160 165 170	
	att agc tgt gtt tgg aac tgc tac cga tac atc aat ggt agg aac tcc	817
35	Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser	

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865	Ser Asp Val Leu Val Tyr Val Ser Asn Asp Thr Val Leu	190	195	200
913	ccc ccg tat gat gat gcc acc gtc aat ggt gcc aag gag cca cgg	205	210	215
913	Pro Pro Tyr Asp Ala Thr Val Asn Gly Ala Lys Glu Pro Pro	220		
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960	Pro Pro Tyr Val Ser Ala			
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2040	gcaacctcc ttgtgttca ttattgatg tgcctgtaaat taagtctgtt gcaattanaa			
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<211> 1380

<210> 113

<213> Homo Sapience

<220>

123/177

&lt;221&gt; CDS

&lt;222&gt; (43)...(630)

&lt;400&gt; 113

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	Met Arg Leu Leu	
	1	
	ctg ctt ctc cta gtg gcg gcg tct gcg atg gtc cgg agc gag gcc tcg	102
	Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Glu Ala Ser	
10	5 10 15 20	
	gcc aat ctg ggc ggc gtg ccc agc aag aga tta aag atg cag tac gcc	150
	Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala	
	25 30 35	
	acg ggg ccg ctg ctc aag ttc cag att tgt gtt tcc tga ggt tat agg	198
15	Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser Xaa Gly Tyr Arg	
	40 45 50	
	cgg gtg ttt gag gag tac atg cgg gtt att agc cag cgg tac cca gac	246
	Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln Arg Tyr Pro Asp	
	55 60 65	
20	atc cgc att gaa gga gag aat tac ctc cct caa cca ata tat aga cac	294
	Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro Ile Tyr Arg His	
	70 75 80	
	ata gca tct ttc ctg tca gtc ttc aaa cta gta tta ata ggc tta ata	342
	Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu Ile Gly Leu Ile	
25	85 90 95 100	
	att gtt ggc aag gat cct ttt gct ttc ttt ggc atg caa gct cct agc	390
	Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met Gln Ala Pro Ser	
	105 110 115	
	atc tgg cag tgg ggc caa gaa aat aag gtt tat gca tgt atg atg gtt	438
30	Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala Cys Met Met Val	
	120 125 130	
	ttc ttc ttg agc aac atg att gag aac cag tgt atg tca aca ggt gca	486
	Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met Ser Thr Gly Ala	
	135 140 145	
35	ttt gag ata act tta aat gat gta cct gtg tgg tct aag ctg gaa tct	534

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35	1	Met Asn	gaaatgctggcgc ctcctggcgcgc ggcgaagggg tggcgcgcgcgc atccgcgcgcgc gcaagcgcgcgc	60
			gactcctggctg cgggcgcgcgc tcttcccccc gagccttgggcgc tgcgcgcgcgc ca atg aac	118
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			atctgttagt taaggtgtca tgccttgacc atcctaataa attgattaat taactgggccc	1340
			tgtgtatctg cgtgtgatta ccagagaaact actaanaaaa ccaactgcct tttaaatcct	1280
			cagatgcgaag atatatgggg aaatccataa ttcagagtaac tctataaat ttgtgtatg	1220
			agagtttacc agaacatcct aatttggcca tgtccagttt atacagttta caaataatag	1160
			ttttttatag tttaaatcg atcccttggg aatccagttg aagttcccaa atactttata	1100
15			aatgtgattt ttttccaaa gattgtcctt aaatcctgtg tgcctttata tgaatatctg	1040
			aaatcctacc ttgttaactt ttttctcagt catattgaa aagtagaana attgagttac	980
			tcccaaccac ccaaaaatcc acccagttaa tgtgtgtgtg tgttttttt tttaaggtaa	920
			cagtgcctgc atatttggg attcctgcac ttcattggagt gcaataatac tgtatagctt	860
			agatgccttc ttggcagcct cgttgttaact cttygaaanaa ctcaatgcga gatagttgtt	800
10			agcagcctga ctgaacttat gaagcctgt actgaagaca gcaagcctgt agtaacagacc	740
			tag caaccactat cagcaactga aactctttg catgaaggga tcatcgcaag	680
		185		
		190		
		195		
			Met Lys Leu Asn Val His Met Asp Ser Ile Pro His His Arg Ser	
5		165		
		170		
		175		
		180		
			Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile Leu Asp Asn Gln	
			ggt cac ctt cca tcc atg caa ctt gtt caa att ctt gac aat gaa	582
		150		
		155		
		160		
			Phe Gln Ile Thr Leu Asn Asp Val Pro Val Trp Ser Lys Leu Gln Ser	

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	Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu Leu	
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	ttg gtg cag ctg ctg cgc ttc ctg agg gct gac ggc gac ctg acg cta	214
5	Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu	
	20 25 30	
	cta tgg gcc gag tgg cag gga cga cgc cca gaa tgg gag ctg act gat	262
	Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp	
	35 40 45 50	
10	atg gtg gtg tgg gtg act gga gcc tcg agt gga att ggt gag gag ctg	310
	Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu	
	55 60 65	
	gct tac cag ttg tct aaa cta gga gtt tct ctt gtg ctg tca gcc aga	358
	Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg	
15	70 75 80	
	aga gtg cat gag ctg gaa agg gtg aaa aga aga tgc cta gag aat ggc	406
	Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly	
	85 90 95	
	aat tta aaa gaa aaa gat ata ctt gtt ttg ccc ctt gac ctg acc gac	454
20	Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp	
	100 105 110	
	act ggt tcc cat gaa gcg gct acc aaa gct gtt ctc cag gag ttt ggt	502
	Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu Phe Gly	
	115 120 125 130	
25	aga atc gac att ctg gtc aac aat ggt gga atg tcc cag cgt tct ctg	550
	Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg Ser Leu	
	135 140 145	
	tgc atg gat acc agc ttg gat gtc tac aga aag cta ata gag ctt aac	598
	Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu Leu Asn	
30	150 155 160	
	tac tta ggg acg gtg tcc ttg aca aaa tgt gtt ctg cct cac atg atc	646
	Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His Met Ile	
	165 170 175	
	gag agg aag caa gga aag att gtt act gtg aat agc atc ctg ggt atc	694
35	Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu Gly Ile	

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180 185 190

ata tct gta cct ctt tcc att gga tac tgt gct agc aag cat gct ctc  
 Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His Ala Leu  
 195 200 205 210

cgg ggt ttt ttt aat ggc ctt cga aca gaa ctt gcc aca tac cga ggt  
 Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly  
 215 220 225

ata ata gtt tct aac att tgc cca gga cct gtc caa tca aat att gtc  
 Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Glu Ser Asn Ile Val  
 230 235 240

gag aat tcc cta gct gga gaa gtc aca aag aat ata ggc aat gat gga  
 Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn Asn Gly  
 245 250 255

gac cag tcc cac aag atg aca acc agt cgt tgc gtc cgg atg tta  
 Asp Glu Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu  
 260 265 270

atc agc atg gcc aat gat tgc aaa gaa gtt tgc atc tca gaa caa cct  
 Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Glu Pro  
 275 280 285 290

tcc tgc tta gta aca tat tgc tgc caa tac atg cca acc tgc gcc tgc  
 Phe Leu Leu Val Thr Tyr Leu Trp Glu Tyr Met Pro Thr Trp Ala Trp  
 295 300 305

tgc ata acc aac aag atg ggg aag aaa agt gtt gag aac ttt aag agt  
 Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe Lys Ser  
 310 315 320

ggt gtc gat gca gac tct tct tat ttt aaa atc ttt aag aca aaa cat  
 Gly Val Asp Ala Asp Ser Tyr Phe Lys Ile Phe Lys Thr Lys His  
 325 330 335

gac tgaagagc atctgtacct ttcagccac tggaggggaaa aatggaaaac a  
 Asp  
 1180

tgaagacagc aatcttctta tgcctctgaa taatcagaag ctaattcttg gtttacctt  
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 1240 1292



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 Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys  
 1 5 10 15  
 cca ggg gag ctg ggg ctt cct cac ccc ctc agc aca gga gga ctc cct 151  
 Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro  
 15 20 25 30  
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 Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val  
 35 40 45  
 acc ccc aag cca ctg gag act gag cct agc agg gag acc gcc tgg tcc 247  
 20 Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser  
 50 55 60  
 ata ggc ctt cag gtg acc gtg ccc ttc atg ttt gca ggc ctg gga ctg 295  
 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu  
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 Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe  
 85 90 95  
 gtg gag gtg aaa gac ctt ttg aca ttg gtg ccg ccc ctg gtg ggc ctg 391  
 Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu  
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 aag ggg aac ctg gag atg aca ctg gca tcc aga ctc tcc aca gct gcc 439  
 Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala  
 115 120 125  
 aac act gga caa att gat gac ccc cag gag cag cac aga gtc atc agc 487  
 35 Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser

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535	agc aac ctg gcc ctg atc cag gtc cag gcc act gtc ggc ggc ctg ggc att cag acc agc cga	130	135	140
583	Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Gly Leu Leu	145	150	155
	gct gct gtc gtc ggc ctg ggc ctg ggc gtc ggc tct cga gag gaa gtc			160
	Ala Ala Val Ala Ala Leu Leu Gly Val Val Ser Arg Gln Val	165	170	175
631	gat gtc gcc aag gtc gag ttg ctg tgt gcc agc agt gtc ctg act gcc			
	Asp Val Ala Lys Val Gln Leu Leu Cys Ala Ser Ser Val Leu Thr Ala	180	185	190
679	ttc ctt gca gcc ttt gcc ctg ggc gtc gtc gtc gtc gtc gtc gtc gtc			
	Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile	195	200	205
727	ggt gct cga aag ctg ggg gtc aac cca gac aac att gcc acc att			
	Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile	210	215	220
775	gca gcc agc ctg gga gac ctg atc aca ctg tcc att ctg gct ttg gtt			
	Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val	225	230	235
823	agc agc ttc ttc tac aga cac aaa gat agt cgg tat ctg acc cgg ctg			
	Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu	245	250	255
871	gtc tgc ctg agc ttt gcc gct ctg acc cca gtc ttg gtc ctg att gcc			
	Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala	260	265	270
919	aaq cag agc cca ccc atc gtc aag atc ctg aag ttt ggc ttg ttc cca			
	Lys Gln Ser Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro	275	280	285
967	atc atc ctg gcc atg gtc atc agc agt ttc gga gga gtc atc ttg agc			
	Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser	290	295	300
1015	aaa acc gtt tct aaa cag tac aaa ggc atg ggc ata ttt acc ccc			
	Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro	305	310	315
1063	gtc ata tgt ggt gtc ggc aat ctg gtc gcc att cag acc agc cga			

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	Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg	
	325 330 335	
	atc tca acc tac ctg cac atg tgg agt gca cct ggc gtc ctg ccc ctc	1111
	Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu	
5	340 345 350	
	cag atg aag aaa ttc tgg ccc aac ccg tgt tct act ttc tgc acg tca	1159
	Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser	
	355 360 365	
	gaa atc aat tcc atg tca gct cga gtc ctg ctc ttg ctg gtg gtc cca	1207
10	Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Leu Val Val Pro	
	370 375 380	
	ggc cat ctg att ttc ttc tac atc atc tac ctg gtg gag ggt cag tca	1255
	Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser	
	385 390 395 400	
15	gtc ata aac agc cag acc ttt gtg gtg ctc tac ctg ctg gca ggc ctg	1303
	Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu	
	405 410 415	
	atc cag gtg aca atc ctg ctg tac ctg gca gaa gtg atg gtt cgg ctg	1351
	Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu	
20	420 425 430	
	act tgg cac cag gcc ctg gat cct gac aac cac tgc atc ccc tac ctt	1399
	Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu	
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	aca ggg ctg ggg gac ctg ctc ggt act ggc ctc ctg gca ctc tgc ttt	1447
25	Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe	
	450 455 460	
	ttc act gac tgg cta ctg aag agc aag gca gag ctg ggt ggc atc tca	1495
	Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser	
	465 470 475 480	
30	gaa ctg gca tct gga cct ccc taactgggcc ccgtgggtcc catttgetca ttag	1550
	Glu Leu Ala Ser Gly Pro Pro	
	485	
	aatttcctct cacatcagtg ggatacagaa ttcagtttct cccttgccag gtccttgga	1610
	tggttgaccc ctgcctctgc agtagccttt tgtgagtctg ctaaggtagc tctcacacac	1670
35	ctcggtctctg gggttgatac ctgagcctgc aatagagccc tgaaatcaag agcatggctt	1730

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1790 gactgtgtga atatgatgtg tgcacatgct taatgagcgt gcaagtgtgc acaagtttgt  
1850 ggaagagagag gtgtctctggc ctgagagagct aagagagagct catgtccagt atgctttgca  
1910 ggggtgtgtt gtctcttcc atgcccagatc aaccagattc ggggtggagc aggaagagagc  
1970 tcttttctgt tcccagagct cagaaacttc gagctgtgga ttaactgtctg tcttcacagc  
2030 gtcacagctc cgtgggcccac actgctgtctg tgcacagagag gtgtacagcc tcccagagat  
2090 gggggcctcat acaacccttc atctgcacatc aacatttatc cgtgtccctg ctgtcttttc  
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Met Arg Thr Leu Phe Asn Leu Leu Trp Leu

1

5

10

gac ctg gcc tgc agc cct gtt cac act acc ctg tca aag tca gat gcc

Ala Leu Ala Cys Ser Pro Val His Thr Thr Leu Ser Lys Ser Asp Ala

15

20

25

aaa aaa gcc gcc tca aag acg ctg gag aag agt cag ttt tca gat

Lys Lys Ala Ala Ser Lys Thr Leu Leu Lys Ser Gln Phe Ser Asp

30

35

40

aag ccg gtc caa gac cgg ggt gtc gtc gtc acg gac ctg aaa gct gag

Lys Pro Val Gln Asp Arg Gly Leu Val Val Thr Asp Leu Lys Ala Gln

45

50

55

agt gtc gtc ctt gag cat cgc agc tac tgc tgc gca aag gcc cgg gac

Ser Val Val Leu Gln His Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp

60

65

70

aga cac ttt gct ggg gat gta ctg ggc tat gtc act cca tgg aac agc

35

350

	Arg His Phe Ala Gly Asp Val Leu Gly Tyr Val Thr Pro Trp Asn Ser	
	75                      80                      85                      90	
	cat ggc tac gat gtc acc aag gtc ttt ggg agc aag ttc aca cag atc	398
	His Gly Tyr Asp Val Thr Lys Val Phe Gly Ser Lys Phe Thr Gln Ile	
5	95                      100                      105	
	tca ccc gtc tgg ctg cag ctg aag aga cgt ggc cgt gag atg ttt gag	446
	Ser Pro Val Trp Leu Gln Leu Lys Arg Arg Gly Arg Glu Met Phe Glu	
	110                      115                      120	
	gtc acg ggc ctc cac gac gtg gac caa ggg tgg atg cga gct gtc agg	494
10	Val Thr Gly Leu His Asp Val Asp Gln Gly Trp Met Arg Ala Val Arg	
	125                      130                      135	
	aag cat gcc aag ggc ctg cac ata gtg cct cgg ctc ctg ttt gag gac	542
	Lys His Ala Lys Gly Leu His Ile Val Pro Arg Leu Leu Phe Glu Asp	
	140                      145                      150	
15	tgg act tac gat gat ttc cgg aac gtc tta gac agt gag gat gag ata	590
	Trp Thr Tyr Asp Asp Phe Arg Asn Val Leu Asp Ser Glu Asp Glu Ile	
	155                      160                      165                      170	
	gag gag ctg agc aag acc gtg gtc cag gtg gca aag aac cag cat ttc	638
	Glu Glu Leu Ser Lys Thr Val Val Gln Val Ala Lys Asn Gln His Phe	
20	175                      180                      185	
	gat ggc ttc gtg gtg gag gtc tgg aac cag ctg cta agc cag aag cgc	686
	Asp Gly Phe Val Val Glu Val Trp Asn Gln Leu Leu Ser Gln Lys Arg	
	190                      195                      200	
	gtg ggc ctc atc cac atg ctc acc cac ttg gcc gag gct ctg cac cag	734
25	Val Gly Leu Ile His Met Leu Thr His Leu Ala Glu Ala Leu His Gln	
	205                      210                      215	
	gcc cgg ctg ctg gcc ctc ctg gtc atc ccg cct gcc atc acc ccc ggg	782
	Ala Arg Leu Leu Ala Leu Leu Val Ile Pro Pro Ala Ile Thr Pro Gly	
	220                      225                      230	
30	acc gac cag ctg ggc atg ttc acg cac aag gag ttt gag cag ctg gcc	830
	Thr Asp Gln Leu Gly Met Phe Thr His Lys Glu Phe Glu Gln Leu Ala	
	235                      240                      245                      250	
	ccc gtg ctg gat ggt ttc agc ctc atg acc tac gac tac tct aca gcg	878
	Pro Val Leu Asp Gly Phe Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala	
35	255                      260                      265	

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926	cat cag cct ggc cct aat gca ccc ctg tcc tgg gtt cga gcc tgc gtc	His Gln Pro Gly Pro Asn Ala Pro Leu Ser Trp Val Arg Ala Cys Val	270	275	280
974	cag gtc ctg gac ccg aag tcc aag tgg cga agc aaa atc ctg ggg	Gln Val Leu Asp Pro Lys Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly	285	290	295
1022	ctc aac ttc tat ggt atg gac tac gcc aac tcc aag gat gcc ggt gag	Leu Asn Phe Tyr Gly Met Asp Tyr Ala Thr Ser Lys Asp Ala Arg Gln	300	305	310
1070	cct gtt gtc ggg gcc aag tac atc cag aca ctg aag gac cac agc ccc	Pro Val Val Gly Ala Arg Tyr Ile Gln Thr Leu Lys Asp His Arg Pro	315	320	325
1118	ccg atg gtc tgg gac agc cag gcc tca gag cac ttc ttc gag tac aag	Arg Met Val Trp Asp Ser Gln Ala Ser Gln His Phe Phe Gln Tyr Lys	335	340	345
1166	aag agc cgc agt ggg aag cac gtc gtc ttc tac cca acc ctg aag tcc	Lys Ser Arg Ser Gly Arg His Val Val Phe Tyr Pro Thr Leu Lys Ser	350	355	360
1214	ctg cag gtc cgg ctg gag ctg gcc cgg gag ggc gtc ggg gtc tct	Leu Gln Val Arg Leu Gln Leu Ala Arg Gln Leu Gly Val Gly Val Ser	365	370	375
1260	atc tgg gag ctg ggc cag ggc ctg gac tac ttc tac gac ctg ctg t	Ile Trp Gln Leu Gln Gly Leu Asp Tyr Phe Tyr Asp Leu Leu	380	385	390
1320	agtgaggcat tgcggcctcc gcggtggacg tgtctcttc taagccatgg agtgagtgag				
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	Glu Ser Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr	
	15 20 25 30	
	ctt gcc ctc ctg ggg ggc ccc acc tgg gca ggg aag atg tat ggc cct	145
	Leu Ala Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro	
10	35 40 45	
	gga gga ggc aag tat ttc agc acc act gaa gac tac gac cat gaa atc	193
	Gly Gly Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile	
	50 55 60	
	aca ggg ctg cgg gtg tct gta ggt ctt ctc ctg gtg aaa agt gtc cag	241
15	Thr Gly Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln	
	65 70 75	
	gtg aaa ctt gga gac tcc tgg gac gtg aaa ctg gga gcc tta ggt ggg	289
	Val Lys Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly	
	80 85 90	
20	aat acc cag gaa gtc acc ctg cag cca ggc gaa tac atc aca aaa gtc	337
	Asn Thr Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val	
	95 100 105 110	
	ttt gtc gcc ttc caa gct ttc ctc cgg ggt atg gtc atg tac acc agc	385
	Phe Val Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser	
25	115 120 125	
	aag gac cgc tat ttc tat ttt ggg aag ctt gat ggc cag atc tcc tct	433
	Lys Asp Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser	
	130 135 140	
	gcc tac ccc agc caa gag ggg cag gtg ctg gtg ggc atc tat ggc cag	481
30	Ala Tyr Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln	
	145 150 155	
	tat caa ctc ctt ggc atc aag agc att ggc ttt gaa tgg aat tat cca	529
	Tyr Gln Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro	
	160 165 170	
35	cta gag gag ccg acc act gag cca cca gtt aat ctc aca tac tca gca	577

175	180	185	190	Leu Glu Pro Thr Thr Glu Pro Val Asn Leu Thr Tyr Ser Ala
175	180	185	190	Asn Ser Pro Val Gly Arg
630	aac tca ccc gtc ggt cgc taggggtggg tatgggggcca tccggagctga ggcga			
195				
690	tctgtgtgtgt ggtggtcgtgat ggtactggag taactgagtc gggagagctga atctggaacc			
711	accataataat aagctctctgc c			

10	<210> 118 <211> 651 <212> DNA <213> Homo Sapiens <220> <221> CDS <222> (242)...(565)	<400> 118
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60	aaagaaacaa gcccgggggac tgcagagccag ggaactcgggc cggcgggggcgg gaaagaaatgg	50
120	ggcagagccgtt ggcceagggccg aagagaccctt gggggtgtgggg gcttgggaatc cgtctcag	40
180	atgagggagag agaggttggag ttgccgggggc tcagggccgg cctcggagcatt gggcggatga	30
240	ggagagtccg gaggccgagggc ctagggtcct tcgggtggag ggagagcggag ccagcggagga	20
286	g atg gag cag aag ctt gtg gag gat ctt caa gca atc atg	10
	Met Glu Glu Lys Leu Val Glu Ile Leu Glu Ala Ile Thr Met	1
		5
		10
		15
334	tca aca gac aca ggt gtt tcc ctt cct tca tat gag gaa gat cag gga	20
	Ser Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Glu Gly	25
		30
382	tca aaa ctc atc cga aag gct aaa gag gca cca ttc gta ccc gtt gga	40
	Ser Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro phe Val Pro Val Gly	45
430	ata gcg ggt ttt gca gca att gtt gca tat gga tta tat aaa ctg aag	50
	Ile Ala Gly phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys	55
		60

478 agc agg gga nat act aaa atg tcc att cat ctg atc cac atg cgt gtg  
35 Ser Arg Gly Asn Thr Lys Met Ser Ile His Leu His Met Arg Val



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	65	70	75	
	gca gcc caa ggc ttt gtt gta gga gca atg act gtt ggt atg ggc tat			526
	Ala Ala Gln Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr			
	80	85	90	95
5	tcc atg tat cgg gaa ttc tgg gca aaa cct aag cct tagaagaa			570
	Ser Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro			
	100	105		
	gagatgctgt cttggtcttg ttggaggagc ttgctttagt tagatgtctt attattaaag			630
	ttacctatta ttgttggaat			651
10				
	<210> 119			
	<211> 1310			
	<212> DNA			
	<213> Homo Sapiens			
15	<220>			
	<221> CDS			
	<222> (78)...(1130)			
	<400> 119			
20	cgaacgccaa ggcggccacg tctgtctccc cctggtgaag aagctgccct gggcttgtcg			60
	tcttagggtc tccagac atg tct gag gtg aag agc cgg aag aag tcg ggg			110
	Met Ser Glu Val Lys Ser Arg Lys Lys Ser Gly			
	1	5	10	
	ccc aag gga gcc cct gct gcg gag ccc ggg aag cgg agc gag ggc ggg			158
25	Pro Lys Gly Ala Pro Ala Ala Glu Pro Gly Lys Arg Ser Glu Gly Gly			
	15	20	25	
	aag acc ccc gtg gcc cgg agc agc gga ggc ggg ggc tgg gca gac ccc			206
	Lys Thr Pro Val Ala Arg Ser Ser Gly Gly Gly Gly Trp Ala Asp Pro			
	30	35	40	
30	cga acg tgc ctg agc ctg ctg tcg ctg ggg acg tgc ctg ggc ctg gcc			254
	Arg Thr Cys Leu Ser Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala			
	45	50	55	
	tgg ttt gta ttt cag cag tca gaa aaa ttt gca aag gtg gaa aac caa			302
	Trp Phe Val Phe Gln Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln			
35	60	65	70	75

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350	tac cag tta ctg aaa cta gaa acc aat gaa ttc caa cta ctt caa agt	350	Tyr Gln Leu Leu Lys Leu Gln Thr Asn Gln Phe Gln Leu Gln Ser	80	85	90	398	aaa atc agt tta atc tca gaa aag tgg cag aaa tct gaa gct atc atg	5	Lys Ile Ser Leu Ile Ser Gln Lys Trp Gln Lys Ser Gln Ala Ile Met	95	100	105	446	gaa caa tgg aag tct ttt caa ata atc gct cat cta aag cgt cta cag	Gln Gln Leu Lys Ser Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln	110	115	120	494	gaa gaa att aat gag gta aaa act tgg tcc aat agg ata act gaa aaa	Gln Gln Ile Asn Gln Val Lys Thr Trp Ser Asn Arg Ile Thr Gln Lys	125	130	135	542	cag gat ata ctg aac aac agt ctg acg acg ctt tct caa gac att aca	Gln Asp Ile Leu Asn Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr	140	145	150	155	590	aaa gta gac caa agt aca act tcc atg gca aaa gat gtt ggt ctc aag	Lys Val Asp Gln Ser Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys	160	165	170	638	att aca agt gta aaa aca gat ata cga cgg att tca ggt tta gta act	Ile Thr Ser Val Lys Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr	175	180	185	686	gat gta ata tca ctg aca gat tct gtg caa gaa cta gaa aat aaa ata	Asp Val Ile Ser Leu Thr Asp Ser Val Gln Gln Leu Gln Asn Lys Ile	190	195	200	734	gag aaa gta gaa aaa aat aca gta aaa aat ata ggt gat ctt ctt tca	Gln Lys Val Gln Lys Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser	205	210	215	782	agc agt att gat cga aca gca acg ctc cga aag aca gca tct gaa aat	Ser Ser Ile Asp Arg Thr Ala Thr Leu Arg Lys Thr Ala Ser Gln Asn	220	225	230	235	830	tca caa aga att aac tct gtt aag aag acg cta acc gaa cta aag agt	Ser Gln Arg Ile Asn Ser Val Lys Lys Thr Leu Thr Gln Leu Lys Ser	240	245	250	878	gac ttc gac aaa cat aca gat aga ttt cta agt tta gaa ggt gac aga	Asp Phe Asp Lys His Thr Asp Arg Phe Leu Ser Leu Gln Gly Asp Arg	255	260	265	878	asp phe asp lys his thr asp arg phe leu ser leu gln gly asp arg	30	35
-----	---	-----	---	----	----	----	-----	---	---	---	----	-----	-----	-----	---	---	-----	-----	-----	-----	---	---	-----	-----	-----	-----	---	---	-----	-----	-----	-----	-----	---	---	-----	-----	-----	-----	---	---	-----	-----	-----	-----	---	---	-----	-----	-----	-----	---	---	-----	-----	-----	-----	---	---	-----	-----	-----	-----	-----	---	---	-----	-----	-----	-----	---	---	-----	-----	-----	-----	---	----	----

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	255	260	265	
	gcc aaa gtt ctg aag aca gtg act ttt gca aat gat cta aaa cca aag			926
	Ala Lys Val Leu Lys Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys			
	270	275	280	
5	gtg tat aat cta aag aag gac ttt tcc cgt tta gaa cca tta gta aat			974
	Val Tyr Asn Leu Lys Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn			
	285	290	295	
	gat tta aca cta cgc att ggg aga ttg gtt acc gac tta cta caa aga			1022
	Asp Leu Thr Leu Arg Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg			
10	300	305	310	315
	gag aaa gaa att gct ttc tta agt gaa aaa ata tct aat tta aca ata			1070
	Glu Lys Glu Ile Ala Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile			
	320	325	330	
	gtc caa gct gag att aag gat att aaa gat gaa ata gca cac att tca			1118
15	Val Gln Ala Glu Ile Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser			
	335	340	345	
	gat atg aat tagtttgaca ttattgagat tagactaagg taattttttt aat			1170
	Asp Met Asn			
	350			
20	gggacctctc atgagaagac tggtaaatca aaaataatga tattttggag caaaagtcac			1230
	tttatattta atcctatttt gtacagtaaa aataaaactt taaaacaggt tgattttcca			1290
	aaataaatat gctaaaacct			1310
	<210> 120			
25	<211> 1400			
	<212> DNA			
	<213> Homo Sapience			
	<220>			
	<221> CDS			
30	<222> (233)...(556)			
	<400> 120			
	tggctgtatg ctattggagg gtggaaatca catctcctgt ttatccgtgt gcttggttagg			60
	tgtcagccgc cccccccccc ccatatgcag atttactcgg catggtagtg gccagcttct			120
35	aacacagctg gtatttcaag tctcctggga cctcactcag gaatgatacc ccctcagtag			180

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235	aagcagcagg tgatctaac tccctcaaa gacgagccct gtcctggagag cc atg	Met	1
283	tcc tca gca ggc aca gca acc cct ctg gaa atg gat cac aaa ctc act	Ser Ser Ala Gly Thr Ala Thr Pro Leu Gln Met Asp His Lys Leu Thr	5
331	tct cag cca ggc aag cca agc ttc tat tgt aac agt agc cac agt ata	Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser Ile	20
379	gtc gga tca tca cat cag ctg ggt ttt tgg ttt agt cat cta gag tcy	Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Gln Ser	35
427	tct gga cta aag gtc ttt cag gtc tcc tcy ccc tgt gag tgc gtc aac	Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Gln Cys Val Asn	40
475	ctc ccc acc cga att gcc tca gtt gtc ctg agc ctc atg tct ctc ctg	Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu Leu	45
523	gtg gtc ggc cag gcc cct gca tgg gaa ggg agc ctg ctg cgg ggc aag	Val Val Gly Gln Ala Pro Ala Trp Gln Gly Ser Leu Leu Arg Gly Arg	70
570	cca gct ggg ggt gct cac cta tgc gca tga tgaattatc gaagcac	Pro Ala Gly Gly Ala His Leu Cys Ala Ala	85
630	tggtgtctga tgtgtgtgag cgtatccctc atggccagcg cgaagtccgc caggtccagcc		90
690	aggtctgcgc aggcctctct ctcggacttg tctctccctg ccaaggggac gtggagaaag		95
750	tgccaggggc cgtccacctgc agccagccctgc tctgctgcct tccctggcag tgtctctggg		100
810	gtgatatccccc taacacctaga tgtccaagcc ctaacttttc ctcaccaaaa ggaagtccag		105
870	ccacgctcgc tctgacctgc caactgtgaca aagtccaagt agcaggtcta ggcacagact		110
930	gggcacatga gcagagggaga cggacccttg agtcttgaca cgaagcgagac cccctccact		115
990	tggtctgggc tggctcctggt ccttaggttt tgtcaggttg tccctgtcttg gatccctcaa		120
1050	ctaggtctga agcacctggag ggggatcgac cgccttgga gttgttctctt aacctccacc		125
1110	atatataatag gccgttggtat ggttgttagag gtaaaagcagg atgatatggtgt tttaaagaca		130
1170	gagctctggga ccaggggctcc taccacctaat ttctctctcc ggttagctgaa caaaggtcta		135
1230	aattagctta acacaaagaa aggtctgcct cagccagaggt tctgaagggc atgcttctcag		140

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tttcccttgt tgacaattgc tctccagttc ctatgaaagc acagagcctt agggggcctg 1290  
 gccacagAAC acaaccatct taggcctgag ctgtgaacag caggggggtg tgtgtctgtt 1350  
 ctgtttctct gcttgccgaa ctttctcaat aaaccctatt tcttatttat 1400

5 <210> 121  
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 <212> PRT  
 <213> Homo sapiens

10 <400> 121  
 Met Lys Ala Phe His Thr Phe Cys Val Val Leu Leu Val Phe Gly Ser  
 1 5 10 15  
 Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Glu Asp Ile Val  
 20 25 30  
 15 Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu Asp  
 35 40 45  
 Ser Val Thr Glu Ser Pro Gln Arg Val Ile Ile Thr Glu Asp Asp Glu  
 50 55 60  
 Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu Gly  
 20 65 70 75 80  
 Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu Pro  
 85 90 95  
 Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr Ser  
 100 105 110  
 25 Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala His  
 115 120 125  
 Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val Thr  
 130 135 140  
 Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys Asn  
 30 145 150 155 160  
 Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu Glu  
 165 170 175  
 Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala Thr  
 180 185 190  
 35 Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu Trp

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35	465	470	475	480
	Gln Lys Lys Leu Gln Lys Lys Met Lys Met Lys Gln Ile Lys Val			
	450	455	460	
	Asp Pro Gln Lys Gln Arg Arg Leu Gln Ala Ala Leu Arg Arg Gln			
	435	440	445	
30	Arg Gln Gln Lys Lys Arg Ala Gln Lys Gln Arg Ile Met Asn Gln Gln			
	420	425	430	
	Phe Leu Lys Leu Thr His Val Gln Arg Gln Ala Ala Gln Ser Arg			
	405	410	415	
	Gln Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Gln Gln Asn			
25	385	390	395	400
	Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn Arg			
	370	375	380	
	Gly Asn Thr Tyr Pro Lys Asp Met Gln Ala Leu Leu Pro Leu Met Asn			
	355	360	365	
20	Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly Ser			
	340	345	350	
	Phe Ser Gly Pro Lys Ile Met Gln Gln Gln Gly Gln Pro Leu Lys Leu			
	325	330	335	
	Leu Thr His Tyr Ala Asp Lys Ile Gln Ser Val His Phe Ser Asp Gln			
15	305	310	315	320
	Met Gly Gln Val Thr Asp Gly Met Met Asp Thr Lys Met Val His Phe			
	290	295	300	
	Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser Gln			
	275	280	285	
10	Gln Lys Gln Met Gln Asp Leu Ser Gln Phe Cys Ser Asp Lys Pro Lys			
	260	265	270	
	Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg Leu			
	245	250	255	
	Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Gln Asp Met			
5	225	230	235	240
	Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg Pro			
	210	215	220	
	Cys Ser Gly Arg Val Cys Cys Gln Gly Met Leu Ile Gln Leu Arg Phe			
	195	200	205	

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Lys Ala Met

&lt;210&gt; 122

&lt;211&gt; 334

5 &lt;212&gt; PRT

&lt;213&gt; Homo sapience

&lt;400&gt; 122

Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg Arg Leu Gln  
 10           1                   5                   10                   15  
 Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala Leu Ala Glu  
                   20                   25                   30  
 Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg Phe Trp Leu  
                   35                   40                   45  
 15 Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg Asp Lys Pro  
           50                   55                   60  
 Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp Thr Ile Trp  
           65                   70                   75                   80  
 Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys Thr Ala Glu  
 20                   85                   90                   95  
 Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro His Gly Val  
                   100                   105                   110  
 Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser Thr Gly Phe  
                   115                   120                   125  
 25 Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met Leu Thr Leu  
           130                   135                   140  
 Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser Ala Gly Leu  
           145                   150                   155                   160  
 Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn Arg Lys Gly  
 30                   165                   170                   175  
 Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln Glu Ala Leu  
                   180                   185                   190  
 Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn Arg Lys Gly  
           195                   200                   205  
 35 Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val Pro Ile Phe

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35	Arg Arg Cys Arg Tyr Cys Leu Val Leu Gln Pro Leu Arg Ala Arg His	85	90	95
30	Gln Leu Lys Gln Gln Gln Thr Ala Met Val Pro Pro Ala Ile Pro Leu Ser Leu Met Asp Pro Gly Tyr Val Asn Val Gln Pro Gln Pro Gln Gln Thr Phe Leu Leu Val Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val	50	55	60
25	Met Ala Pro Trp Ala Leu Leu Ser Pro Gly Val Leu Val Arg Thr Gly His Thr Val Leu Thr Trp Gly Ile Thr Leu Val Leu Phe Leu His Asp Thr Gln Leu Arg Gln Trp Gln Gln Gly Gln Leu Leu Leu Pro Leu	1	5	10
20	<210> 123 <211> 267 <212> PRT <213> Homo sapiens	123	267	
15	Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Gln Phe Cys His Gln Arg Tyr Ile Lys Gln Leu Cys Asn Leu Phe Gln Ala His Lys Gln Val Gln Lys Thr Leu His Pro Ser Gln Gln Val Asn Gln Leu	305	310	315
10	Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly Lys Pro Ile Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr Ser Phe Gly Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile Met Gly Ile	225	230	235
5	Ser Phe Gly Gln Asn Asp Leu Phe Asp Gln Ile Pro Asn Ser Ser Gly Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile Met Gly Ile Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly Lys Pro Ile	245	250	255
	Gln Val Gln Lys Thr Leu His Pro Ser Gln Gln Val Asn Gln Leu His Gln Arg Tyr Ile Lys Gln Leu Cys Asn Leu Phe Gln Ala His Lys Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Gln Phe Cys	260	265	270
	Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr Ser Phe Gly Thr Phe Leu Leu Val Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val Gln Leu Arg Gln Trp Gln Gln Gly Gln Leu Leu Leu Pro Leu	275	280	285
	Thr Gln Leu Arg Gln Trp Gln Gln Gly Gln Leu Leu Leu Pro Leu Thr Phe Leu Leu Val Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val Ser Leu Met Asp Pro Gly Tyr Val Asn Val Gln Pro Gln Pro Gln Gln	290	295	300
	Arg Arg Cys Arg Tyr Cys Leu Val Leu Gln Pro Leu Arg Ala Arg His Gln Leu Lys Gln Gln Gln Thr Ala Met Val Pro Pro Ala Ile Pro Leu Met Ala Pro Trp Ala Leu Leu Ser Pro Gly Val Leu Val Arg Thr Gly	305	310	315
	Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile Met Gly Ile Ser Phe Gly Gln Asn Asp Leu Phe Asp Gln Ile Pro Asn Ser Ser Gly Thr Gln Leu Arg Gln Trp Gln Gln Gly Gln Leu Leu Leu Pro Leu	320	325	330



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	100	105	110
	Cys Arg Glu Cys Arg Arg Cys Val Arg Arg Tyr Asp His His Cys Pro		
	115	120	125
	Trp Met Glu Asn Cys Val Gly Glu Arg Asn His Pro Leu Phe Val Val		
5	130	135	140
	Tyr Leu Ala Leu Gln Leu Val Val Leu Leu Trp Gly Leu Tyr Leu Ala		
	145	150	155
	Trp Ser Gly Leu Arg Phe Phe Gln Pro Trp Gly Leu Trp Leu Arg Ser		
	165	170	175
10	Ser Gly Leu Leu Phe Ala Thr Phe Leu Leu Leu Ser Leu Phe Ser Leu		
	180	185	190
	Val Ala Ser Leu Leu Leu Val Ser His Leu Tyr Leu Val Ala Ser Asn		
	195	200	205
	Thr Thr Thr Trp Glu Phe Ile Ser Ser His Arg Ile Ala Tyr Leu Arg		
15	210	215	220
	Gln Arg Pro Ser Asn Pro Phe Asp Arg Gly Leu Thr Arg Asn Leu Ala		
	225	230	235
	His Phe Phe Cys Gly Trp Pro Ser Gly Ser Trp Glu Thr Leu Trp Ala		
	245	250	255
20	Glu Glu Glu Glu Glu Gly Ser Ser Pro Ala Val		
	260	265	
	<210> 124		
	<211> 106		
25	<212> PRT		
	<213> Homo sapience		
	<400> 124		
	Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro Asn Lys Val Leu		
30	1	5	10
	Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala Leu Asp Asp Pro		15
	20	25	30
	Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly		
	35	40	45
35	Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser		

	50	55	60
the Ile Ser phe Ala Asn Ser Arg Ser Ser Gln Asp Thr Lys Gln Met		70	75
	80		
Met Ser Ser phe Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu	85	90	95
Gln Asn Pro Gln Pro Met Thr Pro Pro Trp	100	105	

<212> PRT  
<213> Homo sapiens

35	40	45
Tyr phe ile Thr Tyr Lys Cys Ser Gly Leu Ser Gln Tyr Asn Ala Phe		
20	25	30
35	40	45
Trp Lys Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys		

	Leu Ile Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu	85	90	95
	Tyr Lys Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile	100	105	110

Met Ser Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe	115	120	125
Asp Trp Lys Tyr Ile Glu Met Ser Ile Asp Ser Asn Ile Ser Leu Val	130	135	140

130	135	140	His Tyr Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp
145	150	155	160
35	Leu Tyr His Thr Phe Arg Pro Ala Val Leu Leu Met Phe Leu Ser		

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165 170 175  
 Val Tyr Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu  
 180 185 190  
 Gly Ser Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu  
 5 195 200 205  
 Ala Leu Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser  
 210 215 220  
  
 <210> 126  
 10 <211> 258  
 <212> PRT  
 <213> Homo sapience  
  
 <400> 126  
 15 Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val Tyr Ser Val Pro Arg  
 1 5 10 15  
 Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu Leu Ser Ala Leu Leu  
 20 25 30  
 Ser Ala Ala Phe Leu Leu Val Arg Lys Leu Pro Pro Leu Cys His Gly  
 35 40 45  
 20 Leu Pro Thr Gln Arg Glu Asp Gly Asn Pro Cys Asp Phe Asp Trp Arg  
 50 55 60  
 Glu Val Glu Ile Leu Met Phe Leu Ser Ala Ile Val Met Met Lys Asn  
 65 70 75 80  
 25 Arg Arg Ser Met Phe Leu Met Thr Cys Lys Pro Pro Leu Tyr Met Gly  
 85 90 95  
 Pro Glu Tyr Ile Lys Tyr Phe Asn Asp Lys Thr Ile Asp Glu Glu Leu  
 100 105 110  
 Glu Arg Asp Lys Arg Val Thr Trp Ile Val Glu Phe Phe Ala Asn Trp  
 115 120 125  
 30 Ser Asn Asp Cys Gln Ser Phe Ala Pro Ile Tyr Ala Asp Leu Ser Leu  
 130 135 140  
 Lys Tyr Asn Cys Thr Gly Leu Asn Phe Gly Lys Val Asp Val Gly Arg  
 145 150 155 160  
 35 Tyr Thr Asp Val Ser Thr Arg Tyr Lys Val Ser Thr Ser Pro Leu Thr

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35	<210> 128	
30	Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val His Val Tyr 100 105 110	
25	Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly Gly Leu Phe Thr Tyr 85 90 95	
20	Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn Lys Tyr Phe Lys Ser 65 70 75 80	
15	Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser Val Leu Ser Leu 50 55 60	
10	Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile Leu Gly Leu Thr Gly 35 40 45	
5	Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp Tyr Cys Arg Thr Ser 20 25 30	
	Met Ala Ala Val Val Ala Lys Arg Gln Gly Pro Pro Phe Ile Ser Gln 1 5 10 15	
	<400> 127	
	<213> Homo sapiens	
	<212> PRT	
	<211> 110	
	<210> 127	
	Asp Lys	
10	Pro Val Ala Ser Thr Pro Thr Thr Val Ser Asp Gly Gln Asn Lys Lys 245 250 255	
5	Arg Ala Lys Lys Leu Ser Lys Ala Gly Asp Asn Ile Pro Gln Gln 225 230 235 240	
	Ser Gln Gln Asn Val Ile Arg Gln Phe Asn Leu Asn Gln Tyr Gln 210 215 220	
	Arg Arg Pro Gln Ile Asp Lys Lys Gly Arg Ala Val Ser Trp Thr Phe 195 200 205	
	Lys Gln Leu Pro Thr Leu Ile Leu Phe Gln Gly Gly Lys Gln Ala Met 180 185 190	
	165 170 175	

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&lt;211&gt; 91

&lt;212&gt; PRT

&lt;213&gt; Homo sapience

5 &lt;400&gt; 128

Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser Gln Ser

1 5 10 15

Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile Ala Glu

20 25 30

10 Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val Lys Lys

35 40 45

Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp Gly Arg

50 55 60

Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn His Leu

15 65 70 75 80

Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly

85 90

&lt;210&gt; 129

20 &lt;211&gt; 344

&lt;212&gt; PRT

&lt;213&gt; Homo sapience

&lt;400&gt; 129

25 Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser

1 5 10 15

Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu

20 25 30

Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val

30 35 40 45

Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys

50 55 60

Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe

65 70 75 80

35 Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu

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85 90 95

Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Ile Gln  
100 105 110

Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser  
115 120 125

Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser  
130 135 140

Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr  
145 150 155

Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly  
165 170 175

Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys  
180 185 190

Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser  
195 200 205

Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Gln Pro Ile Phe Ser Ser  
210 215 220

Ser Gln Pro Thr Ser Gln Ala Arg Ile Gly Met Gly Ala Thr Leu Asp  
225 230 235

Ile Gln Arg Gln Gln Arg Met Gln Leu Leu Asp Arg Gln Leu Met Phe  
245 250 255

Ser Gln Phe Ala Gln Gly Arg Gln Arg Gln Gln Gln Gly Gly Met  
260 265 270

Ile Asn Trp Asn Arg Leu Phe Pro Leu Arg Gln Arg Gln Asn Val  
275 280 285

Asn Tyr Gln Gly Gly Arg Gln Ser Gln Pro Ala Ala Pro Leu Gln  
290 295 300

Val Ser Gln Gln Val Ala Arg Leu Met Gln Met Gly Phe Ser Arg  
305 310 315

Gly Asp Ala Leu Gln Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val  
325 330 335

Ala Thr Asn Phe Leu Leu Gln His

340

35 <210> 130

149/177

&lt;211&gt; 428

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

5 &lt;400&gt; 130

Met Gly Pro Pro Pro Gly Ala Gly Val Ser Cys Arg Gly Gly Cys Gly  
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 10 Ala Pro Gly Ser Arg Gly Ala Glu Ala Val Trp Thr Ala Tyr Leu Asn  
 35 40 45  
 Val Ser Trp Arg Val Pro His Thr Gly Val Asn Arg Thr Val Trp Glu  
 50 55 60  
 Leu Ser Glu Glu Gly Val Tyr Gly Gln Asp Ser Pro Leu Glu Pro Val  
 15 65 70 75 80  
 Ala Gly Val Leu Val Pro Pro Asp Gly Pro Gly Ala Leu Asn Ala Cys  
 85 90 95  
 Asn Pro His Thr Asn Phe Thr Val Pro Thr Val Trp Gly Ser Thr Val  
 100 105 110  
 20 Gln Val Ser Trp Leu Ala Leu Ile Gln Arg Gly Gly Gly Cys Thr Phe  
 115 120 125  
 Ala Asp Lys Ile His Leu Ala Tyr Glu Arg Gly Ala Ser Gly Ala Val  
 130 135 140  
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 Pro Gly Ala Val Asp Ile Val Ala Ile Met Ile Gly Asn Leu Lys Gly  
 165 170 175  
 Thr Lys Ile Leu Gln Ser Ile Gln Arg Gly Ile Gln Val Thr Met Val  
 180 185 190  
 30 Ile Glu Val Gly Lys Lys His Gly Pro Trp Val Asn His Tyr Ser Ile  
 195 200 205  
 Phe Phe Val Ser Val Ser Phe Phe Ile Ile Thr Ala Ala Thr Val Gly  
 210 215 220  
 Tyr Phe Ile Phe Tyr Ser Ala Arg Arg Leu Arg Asn Ala Arg Ala Gln  
 35 225 230 235 240

Ser Arg Lys Gln Arg Gln Leu Lys Ala Asp Ala Lys Lys Ala Ile Gly

Arg Len Gln Leu Arg Thr Leu Lys Gln Gly Asp Lys Gln Ile Gly Pro

asp Gly asp Ser Cys Ala Val Cys Ile Glu Leu Tyr Lys Pro Asn Asp

Leu Val Arg Ile Leu Thr Cys Asn His Ile Phe His Lys Thr Cys Val

asp pro trp leu leu glu his arg thr cys pro met cys lys cys asp

ITL LBN LYS ALB LBN GLY ITL GLN VAL ASP VAL GLN ASP GLY SER VAL

ser teu gln val pro val ser asn glu ile ser asn ser ala ser ser

THIS END GUARD ASP. ARG. SET. GUIN. THE. ALA. SET. SET. GUY. TYR. ALA. SET.

THE UNITED STATES DEPARTMENT OF JUSTICE  
WASHINGTON, D. C. 20535

TRA RIW TRA TAS USW RIW DIO SIW USW TRA DAT UIO DAT TAS DIO USW

THE

100 618 011 270 674 124 274 711 210 470 200 011

121

1115 1116

03

at a distance of 100 m from the shore. The water depth was 10 m. The water temperature was 20°C. The water was clear and the visibility was good. The water was calm and the wind was light. The water was clear and the visibility was good. The water was calm and the wind was light.

1. **Identify the main components of the system.**  
 2. **Define the scope and objectives of the study.**  
 3. **Review the literature related to the topic.**  
 4. **Develop a methodology for data collection and analysis.**  
 5. **Collect and analyze the data.**  
 6. **Draw conclusions and discuss the implications of the findings.**  
 7. **Write the report and present the results.**

၁၁၇၁၁၇၁၁၁၁ ၁၁၁၁၁၁၁၁၁၁ ၁၁၁၁၁၁၁၁၁၁ ၁၁၁၁၁၁၁၁၁၁ ၁၁၁၁၁၁၁၁၁၁ ၁၁၁၁၁၁၁၁၁၁



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	ttgatgggtga ctggtctgct tgcttatatc atgaattaca tcattgggaa gaataaaaac	480
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	cggaaactaca ttgcgggctt ccccccctat ggagtcctgg cagtcggagc ctttgccaac	360
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153/177

&lt;213&gt; Homo sapience

&lt;400&gt; 134

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&lt;210&gt; 135

&lt;211&gt; 672

&lt;212&gt; DNA

&lt;213&gt; Homo sapience

15

&lt;400&gt; 135

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 tttgttatgg agaccttcgt ccacctctgc tgcgtgggca gttgggcagc tctactggcc 600  
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 aatgtgcact cc 672

30

&lt;210&gt; 136

&lt;211&gt; 774

&lt;212&gt; DNA

&lt;213&gt; Homo sapience

35

&lt;400&gt; 136

154/177

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25	<210> 137 <211> 330 <212> DNA <213> Homo sapiens	atggcgcggg tgggtggcga ggggaaagg ccggcgttca tcagcggagg ggcgttgagg ggcaagccgg ccgtccctgga ttattggcgg acctcgggtg cagcggctgtc gggggccacg ggcggacacc tcggcctcac cggcctcac ggccttcacat tcacaccgtc cggcctcgtc ctgcctcccc tgcctcccat tctcaaggcg ggagggaggtt ggaacaaataa ttccaacaa cggagacacc tctttacaagg aggcctcacatc ggggggcctc tcacaccagc cctgttctgg
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Ser Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Glu Asp Ile

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gta gag tat gat gat aat gac ttc gct gaa ttt gag gat gtc atg gaa 262

Val Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu

35 40 45

gac tct gtt act gaa tct cct caa cgg gtc ata atc act gaa gat gat 310

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50 55 60

gaa gat gag acc act gtg gag ttg gaa ggg cag gat gaa aac caa gaa 358

Glu Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu

65 70 75

15 gga gat ttt gaa gat gca gat acc cag gag gga gat act gag agt gaa 406

Gly Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu

80 85 90 95

cca tat gat gat gaa gaa ttt gaa ggt tat gaa gac aaa cca gat act 454

Pro Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr

20 100 105 110

tct tct agc aaa aat aaa gac cca ata acg att gtt gat gtt cct gca 502

Ser Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala

115 120 125

cac ctc cag aac agc tgg gag agt tat tat cta gaa att ttg atg gtg 550

25 His Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val

130 135 140

act ggt ctg ctt gct tat atc atg aat tac atc att ggg aag aat aaa 598

Thr Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys

145 150 155

30 aac agt cgc ctt gca cag gcc tgg ttt aac act cat agg gag ctt ttg 646

Asn Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu

160 165 170 175

gag agc aac ttt act tta gtg ggg gat gat gga act aac aaa gaa gcc 694

Glu Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala

35 180 185 190

[illegible]



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	370	375	380	
	aac atg gtg att tat tct att gat aaa gcc aaa aag ttc cga ctc aac			1318
	Asn Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn			
	385	390	395	
5	aga gaa ggc aaa caa aaa gca gat aag aac cgt gcc cga gta gaa gag			1366
	Arg Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu			
	400	405	410	415
	aac ttc ttg aaa ctg aca cat gtg caa aga cag gaa gca gca cag tct			1414
	Asn Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser			
10	420	425	430	
	cgg cgg gag gag aaa aaa aga gca gag aag gag cga atc atg aat gag			1462
	Arg Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu			
	435	440	445	
	gaa gat cct gag aaa cag cgc agg ctg gag gag gct gca ttg agg cgt			1510
15	Glu Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg			
	450	455	460	
	gag caa aag aag ttg gaa aag aag caa atg aaa atg aaa caa atc aaa			1558
	Glu Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys			
	465	470	475	
20	gtg aaa gcc atg taaagccatc ccagagattt gagttctgat gccacctgta			1610
	Val Lys Ala Met			
	480			
	agctctgaat tcacaggaaa catgaaaaac gccagtcctat ttctcaacct taaatttcag			1670
	acagtcttgg gcaactgaga aatcettatt tcatcatcta ctctgtttgg ggtttgggt			1730
25	tttacagaga ttgaagatac ctggaaaggg ctctgtttca agaatttttt ttccagata			1790
	atcaaattat tttgattatt ttataaaagg aatgatctat gaaatctgtg taggttttaa			1850
	atattttaaa aattataata caaatcatca gtgcttttag tacttcagtg tttaaagaaa			1910
	taccatgaaa tttataggta gataaccaga ttgttgcttt ttgttttaaac caagcagttg			1970
	aaatggctat aaagactgac tctaaaccaa gattctgcaa ataatgattg gaattgcaca			2030
30	ataaacattg cttgatgttt			2050
	<210> 142			
	<211> 2746			
	<212> DNA			
35	<213> Homo sapience			

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<220>  
<221> CDS  
<222> (70)...(1074)  
<400> 142

60 aaaaacctgtg ggtgacctcag accacagcag agctcacaga acctgaggga gccaggtcta  
108 ccgcgcagc atg gta gag ttc gcg ccc ttg ttt atg ccg tgg gag cgc  
Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg

10 agg ctg cag aca ctt gct gtc cta cag ttt gtc ttc ttc ttg gca  
156 Arg Leu Glu Thr Leu Ala Val Leu Glu Phe Val Phe Ser Phe Leu Ala  
20 15  
25 20  
25 25

15 Leu Ala Glu Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg  
204 ctg gcc gag atc tgc act gtc gag ttc ata gcc ctc ctg ttt aca aga  
30 35 40 45

20 ttc tgg ctc ctc act gtc ttc tat ggc gcc tgg tgg tat ctg gag cga  
252 Phe Trp Leu Leu Thr Val Leu Tyr Ala Trp Trp Tyr Leu Asp Arg  
300 50 55 60

20 gag aag cca cag cag ggg ggc cag cac atc cag gcc atc agt tgc tgg  
300 Asp Lys Pro Arg Glu Gly Gly Arg His Ile Glu Ala Ile Arg Cys Trp  
348 65 70 75

25 act ata tgg aag tac atg aag gac tat ttc ccc atc tcc ctg gtc aag  
348 Thr Ile Trp Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys  
396 80 85 90

25 act gct gag ctg gag ccc tct ccg aac tac atc ggc ggc ttc cac ccc  
396 Thr Ala Glu Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro  
444 95 100 105

30 cat gga gtc ctg gca gtc gga gcc ttc gcc aac ctg tgc act gag agc  
444 His Gly Val Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser  
492 110 115 120 125

35 aca ggc ttc tct tcc atc ttc ccc ggt atc cgc ccc cat ctg atg atg  
492 Thr Gly Phe Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met  
540 130 135 140

35 ctg acc ttg tgg ttc ccg gcc ccc ttc ttc aga gat tac atc atg tct  
540 Leu Thr Leu Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser

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	145	150	155	
	gca ggg ttg gtc aca tca gaa aag gag agt gct gct cac att ctg aac	588		
	Ala Gly Leu Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn			
	160	165	170	
5	agg aag ggt ggc gga aac ttg ctg ggc atc att gta ggg ggt gcc cag	636		
	Arg Lys Gly Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln			
	175	180	185	
	gag gcc ctg gat gcc agg cct gga tcc ttc acg ctg tta ctg cgg aac	684		
	Glu Ala Leu Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn			
10	190	195	200	205
	cga aag ggc ttc gtc agg ctc gcc ctg aca cac ggg gca ccc ctg gtg	732		
	Arg Lys Gly Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val			
	210	215	220	
	cca atc ttc tcc ttc ggg gag aat gac cta ttt gac cag att ccc aac	780		
15	Pro Ile Phe Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn			
	225	230	235	
	tct tct ggc tcc tgg tta cgc tat atc cag aat cgg ttg cag aag atc	828		
	Ser Ser Gly Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile			
	240	245	250	
20	atg ggc atc tcc ctc cca ctc ttt cat ggc cgt ggt gtc ttc cag tac	876		
	Met Gly Ile Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr			
	255	260	265	
	agc ttt ggt tta ata ccc tac cgc cgg ccc atc acc act gtg gtg ggg	924		
	Ser Phe Gly Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly			
25	270	275	280	285
	aag ccc atc gag gta cag aag acg ctg cat ccc tcg gag gag gag gtg	972		
	Lys Pro Ile Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Glu Val			
	290	295	300	
	aac cag ctg cac cag cgt tat atc aaa gag ctg tgc aac ctc ttc gag	1020		
30	Asn Gln Leu His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu			
	305	310	315	
	gcc cac aaa ctt aag ttc aac atc cct gct gac cag cac ttg gag ttc	1068		
	Ala His Lys Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe			
	320	325	330	
35	tgc tgagcccaa agggcagggc caacattagg gagcccagca ggaggtgctg	1120		

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Cys

1180 tgcctgagag aactccctgga ggtgtcttctt gaaacatctt ccagagacct ccagagacct  
1240 tgcgaatcca acccatatca ggcctgttaagt cagagcagagc aatgcagagag agagagacag  
1300 accaaggggt cagctggggc taaggacagt aggcctgcta agggggctgg gctctctt  
1360 gacatggac actggggccc tctctatctt agtctgtctg ttacatctca ttgttggctg  
1420 atccaaag atgagagcca aagctgagag gactcagatc ctatggctgc caactcaca  
1480 gcatctctc tacttgcatc ttgttgctcg aagcagtcac aaccagcag atccaaagag  
1540 taaggatatg gatccccccc ttgatgggag gagcagcat gtcatatcac aaaaagggtgt  
1600 ggaacacatgc agggatctt actgacct ttgcacacaa tccacacaaa cttaaaact  
1660 aagacctga agcacaagca ctccacaccc caggcacaca caccctggaa ttccctgtgt  
1720 gaccatgtta ccaacactgt gttctccagg gatccagctc cagcttgcga tgcctggccc  
1780 atccctctc cgtctctccc ttgttgatccc tactgacag ccacagcggag ctgtctaaaa  
1840 caaagaacct accgacctat ttccatctca gcatctccc atgacacctc attgctctca  
1900 gatatagggt ttgacacagt ttgaatccaga ggtcatagat ccagcagggaa ccagaggtata  
1960 atctgagag ggtttaaaaa ggaaacctt ttctgaggtgt ttgcacctgt tccacacctga  
2020 ggcctggaaag gattgaaatgga agcagcagtt cctgaaacag gaaagacatcat gttgtggggg  
2080 catctgctgt caaagggtcc gaacaggtct gttgacacct caaagggtgga gccaaaggaca  
2140 agcatccca ctccacctc ctccatctca ttctgctgca agtctcccca ttgcctggagc  
2200 caactagag cttgagggga agagggctgt ttgcttgagc ccagcagatgt aggcctccct  
2260 ggaagggag aatggcagaag acagcagag ttgatactga ggggtcacag gaaagacggaa  
2320 catgtccact tccagggccc agctctcag acctctctt gccacatccc agcatctggc  
2380 ccagctgtc catccctcat tctctctccc ctctacccc ttgctccccc aactcgggaa  
2440 atctgcattt ctctgtctca gctatatctgt ctcaacctcg agttcttctg catgagtgtg  
2500 gatgcacatg aatgcacatc cctcccccct atcccccct ttgtcttgatc atctctactc  
2560 atcccaaat actgattta tctgtgcaaa gaagctctcc ccagttgctc ttgttgacag  
2620 ggttctctc ttgctctccc agacttctcg ttccctcaca accagccctta gcccccctgg  
2680 gagggaggtgt ttgtgtccag gtaaatgtcg cgcacatgcc cctggcctca gttgcacctccc  
2740 tccagctcac ccacaaaaag gacctgcatc ctgtctcaca aataaaaaatg aactcttgaa  
2746 atggtg

5

10

15

20

25

30

35

<210> 143

<211> 1136

<212> DNA

<213> Homo sapiens

<220>

163/177

&lt;221&gt; CDS

&lt;222&gt; (32)...(835)

&lt;400&gt; 143

5	atttcttcggtgtggggccccgggcccagagggcgatggcgccctggcgctcctc	52
	Met Ala Pro Trp Ala Leu Leu	
	1 5	
	agc cct ggg gtc ctg gtg cgg acc ggg cac acc gtg ctg acc tgg gga	100
	Ser Pro Gly Val Leu Val Arg Thr Gly His Thr Val Leu Thr Trp Gly	
10	10 15 20	
	atc acg ctg gtg ctc ttc ctg cac gat acc gag ctg cgg caa tgg gag	148
	Ile Thr Leu Val Leu Phe Leu His Asp Thr Glu Leu Arg Gln Trp Glu	
	25 30 35	
	gag cag ggg gag ctg ctc ctg ccc ctc acc ttc ctg ctc ctg gtg ctg	196
15	Glu Gln Gly Glu Leu Leu Leu Pro Leu Thr Phe Leu Leu Leu Val Leu	
	40 45 50 55	
	ggc tcc ctg ctg ctc tac ctc gct gtg tca ctc atg gac cct ggc tac	244
	Gly Ser Leu Leu Leu Tyr Leu Ala Val Ser Leu Met Asp Pro Gly Tyr	
	60 65 70	
20	gtg aat gtg cag ccc cag cct cag gag gag ctc aaa gag gag cag aca	292
	Val Asn Val Gln Pro Gln Pro Gln Glu Glu Leu Lys Glu Glu Gln Thr	
	75 80 85	
	gcc atg gtt cct cca gcc atc cct ctt cgg cgc tgc aga tac tgc ctg	340
	Ala Met Val Pro Pro Ala Ile Pro Leu Arg Arg Cys Arg Tyr Cys Leu	
25	90 95 100	
	gtg ctg cag ccc ctg agg gct cgg cac tgc cgt gag tgc cgc cgt tgc	388
	Val Leu Gln Pro Leu Arg Ala Arg His Cys Arg Glu Cys Arg Arg Cys	
	105 110 115	
	gtc cgc cgc tac gac cac cac tgc ccc tgg atg gag aac tgt gtg gga	436
30	Val Arg Arg Tyr Asp His His Cys Pro Trp Met Glu Asn Cys Val Gly	
	120 125 130 135	
	gag cgc aac cac cca ctc ttt gtg gtc tac ctg gcg ctg cag ctg gtg	484
	Glu Arg Asn His Pro Leu Phe Val Val Tyr Leu Ala Leu Gln Leu Val	
	140 145 150	
35	gtg ctt ctg tgg ggc ctg tac ctg gca tgg tca ggc ctc cgg ttc ttc	532

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35	<221> CDS	
	<220>	
	<213> Homo sapiens	
	<212> DNA	
	<211> 619	
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	atttatata aagcaagtc agtcct	1136
	agcagagccccc gggtctccacc ccaagccccc ccaaggtgct gccagtgca acatttaca	1110
	ggcagttctg cctcccaagg aagaaaggga agaaagagac ctgtgggtgg ctcaaggcca	1050
25	tgcccaagccc tcccaagacc cagaaaggag ctccaagtc aagagatccc tgccttggtg	990
	aaacacaggg gctgtccccc agctgggtg agcgtccaga gggtccgggg cctccactcc	930
	265	
	Ser Pro Ala Val	
	agc cca gct gtt taggtgtgct ggaagccggg ctacgtctt gtgctga	870
20	250	
	Ser Gly Ser Trp Gln Thr Leu Trp Ala Gln Gln Gln Gly Ser	
	tca ggg tcc tgg gag acc ctc tgg gct gag gag gag gag ggc agc	820
	235	
	240	
	245	
15	gac cga ggc ctg acc cgc aac ctg gcc cac ttc tgc tga tgg ccc	772
	220	
	225	
	230	
	Ser Ser His Arg Ile Ala Tyr Leu Arg Gln Arg Pro Ser Asn Pro Phe	
	tcc tca cac cgc atc gcc tat ctc cgc cag gcc acc agc ccc ttc	724
	200	
	205	
	210	
	215	
10	Ser His Leu Tyr Leu Val Ala Ser Asn Thr Thr Trp Gln Phe Ile	
	tgc cac ctc tac ctg gtc gcc acc acc acc acc acc tgg gaa ttc atc	676
	185	
	190	
	195	
	Phe Leu Leu Ser Leu Phe Ser Leu Val Ala Ser Leu Leu Val	
	tcc ctg ctg tcc ctc tcc tgc tgg gcc agc ctg ctc gtc	628
	170	
	175	
	180	
5	Gln Pro Trp Gly Leu Trp Leu Arg Ser Gly Leu Leu Phe Ala Thr	
	cag ccc tgg ggt ctg tgg tgc agc ggg ctc ctg ttc gcc acc	580
	155	
	160	
	165	
	Val Leu Leu Trp Gly Leu Tyr Leu Ala Trp Ser Gly Leu Arg Phe	

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&lt;222&gt; (13)...(333)

&lt;400&gt; 144

5                    Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro  
                          1                    5                    10  
 aac aaa gtg ctg agg tac aag ccc ccg ccg agc gaa tgt aac ccg gcc                    96  
 Asn Lys Val Leu Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala  
                          15                    20                    25  
 10                    ttg gac gac ccg acg ccg gac tac atg aac ctg ctg ggc atg atc ttc                    144  
 Leu Asp Asp Pro Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe  
                          30                    35                    40  
 agc atg tgc ggc ctc atg ctt aag ctg aag tgg tgt gct tgg gtc gct                    192  
 Ser Met Cys Gly Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala  
 15                    45                    50                    55                    60  
 gtc tac tgc tcc ttc atc agc ttt gcc aac tct ccg agc tgc gag gac                    240  
 Val Tyr Cys Ser Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp  
                          65                    70                    75  
 acg aag caa atg atg agt agc ttc atg ctg tcc atc tct gcc gtg gtg                    288  
 20                    Thr Lys Gln Met Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val  
                          80                    85                    90  
 atg tcc tat ctg cag aat cct cag ccc atg acg ccc cca tgg                    340  
 Met Ser Tyr Leu Gln Asn Pro Gln Pro Met Thr Pro Pro Trp  
                          95                    100                    105  
 25                    tgataaccagc ctagaagggt cacatcttgg accctgtcta tccactagge ctgggctttg                    390  
 gctgctaaac ctgctgcctt cagctgcat cctggacttc cctgaatgag gccgtctcgg                    450  
 tgccccagc tggatagagg gaacctggcc ctttcctagg gaacacccta ggcttaccoc                    510  
 tcctgcctcc cttccctgc ctgctgctgg gggagatgct gtccatgttt ctagggttat                    570  
 tcatttgctt tctcgttgaa acctgttgtt aataaagttt ttcactcag                    619  
 30  
 <210> 145  
 <211> 864  
 <212> DNA  
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 35                    <220>

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<221> CDS  
<222> (111)...(785)

<400> 145

5 agtgggtgc cagccctgg cgtggcgaa agagccggcg gagccggaga ccgctcccg  
116 gagagccgc ctcgcatcc ccgcccgggc ggagccgggc ggccggcatc atg acc  
Met Thr  
1

164 ctg ttc cac ttc ggc aac tgc tgc gct ctt gcc tac ttc ccc tac ttc  
10 Leu phe his phe gly asn cys phe ala leu ala tyr phe pro tyr phe  
5 10 15

212 atc acc tac aag tgc agc ggc ctg tcc gag tac aac gcc ttc tgg aaa  
Ile thr tyr lys cys ser gly leu ser glu tyr asn ala phe trp lys  
20 25 30

260 tgc gtc cag gct gga gtc acc tac ctc ttc gtc caa ctc tgc aag atg  
Cys val gln ala gly val thr tyr leu phe val gln leu cys lys met  
35 40 45 50

308 ctg ttc tgc gcc act ttc ccc acc tgg gaa ggc ggc atc tat gac  
Leu phe leu ala thr phe pro thr trp glu gly ile tyr asp  
55 60 65

356 ttc att ggg gag ttc atg aag gcc agc gtc gat gtc gca gac ctg ata  
phe ile gly glu phe met lys ala ser val asp val ala asp leu ile  
70 75 80

404 ggt cta aac ctt gtc atg tcc ccg aat gcc ggc aag gga gag tac aag  
gly leu asn leu val met ser arg asn ala gly lys gly glu tyr lys  
85 90 95

452 atc atg gtc gct gcc ctg ggc acc gct gag ctt att atg tcc  
Ile met val ala ala leu gly trp ala thr ala glu leu ile met ser  
100 105 110

500 cgc tgc att ccc cta tgg gtc gga gcc ccg ggc att gag ttt gac tgg  
arg cys ile pro leu trp val gly ala arg gly ile glu phe asp trp  
115 120 125 130

548 aag tac atc cag atg agc ata gac tcc aac atc agt ctg gtc cat tac  
lys tyr ile gln met ser ile asp ser asn ile ser leu val his tyr  
135 140 145

35

30

25

20

15

10

5



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atc gtc gcg tct gct cag gtc tgg atg ata aca cgc tat gat ctg tac 596  
 Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp Leu Tyr  
 150 155 160  
 cac acc ttc cgg cca gct gtc ctc ctg ctg atg ttc ctc agt gtc tac 644  
 5 His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser Val Tyr  
 165 170 175  
 aag gcc ttt gtt atg gag acc ttc gtc cac ctc tgc tcg ctg ggc agt 692  
 Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu Gly Ser  
 180 185 190  
 10 tgg gca gct cta ctg gcc cga gca gtg gta acg ggg ctg ctg gcc ctc 740  
 Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu Ala Leu  
 195 200 205 210  
 agc act ttg gcc ctg tat gtc gcc gtt gtc aat gtg cac tcc taggettg 790  
 Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser  
 15 215 220  
 gtgtctcaga cattgatgta ccttttccct gcctcgctcc aggttttagt gaagtaaaca 850  
 gtatttgga agtt 864  
  
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 20 <211> 1527  
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 <213> Homo sapience  
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 25 <222> (25)...(801)  
  
 <400> 146  
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 Met Ala Val Leu Ala Pro Leu Ile Ala  
 1 5  
 30 ctc gtg tat tcg gtg ccg cga ctt tca cga tgg ctc gcc caa cct tac 99  
 Leu Val Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr  
 10 15 20 25  
 tac ctt ctg tcg gcc ctg ctc tct gct gcc ttc cta ctc gtg agg aaa 147  
 35 Tyr Leu Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys

35	723	<p>           nac tta aat gag cta tac cag cgg gcc aag aaa cta tca aag gct gga            205            210            215            Arg Ala Val Ser Trp Thr Phe Ser Gln Gln Asn Val Ile Arg Gln Phe            675         </p>
30	627	<p>           cgg gct gtc tca tgg acc ttc tct gag gag aat gtc atc cga gaa ttc            190            195            200            Gln Gly Gly Lys Gln Ala Met Arg Arg Pro Gln Ile Asp Lys Gly            627         </p>
25	579	<p>           caa ggt ggc aag gag gca atg cgg cga cag att gac aag aaa gga            170            175            180            185            Val Ser Thr Ser Pro Leu Thr Lys Gln Leu Pro Thr Leu Ile Leu Phe            579         </p>
20	531	<p>           gty agc aca tca ccc ctc acc aag caa ctc cct acc ctg atc ctg ttc            155            160            165            Gly Lys Val Asp Val Gly Arg Tyr Thr Asp Val Ser Thr Arg Tyr Lys            531         </p>
15	483	<p>           ggg aag gty gat gtc gga cgc tat act gat gtt agt acc cgg tac aaa            140            145            150            Ile Tyr Ala Asp Leu Ser Leu Lys Tyr Asn Cys Thr Gly Leu Asn Phe            483         </p>
10	435	<p>           atc tat gct gac ctc tcc ctt aaa tac aac tgt aca ggg cta aat ttc            125            130            135            Val Gln Phe Phe Ala Asn Trp Ser Asn Asp Cys Gln Ser Phe Ala Pro            435         </p>
5	387	<p>           gty gag ttc ttt gcc aat tgg tct aat gac tgc caa tca ttt gcc cct            110            115            120            Lys Thr Ile Asp Gln Gln Leu Gln Arg Asp Lys Arg Val Thr Trp Ile            387         </p>
	339	<p>           aaa acc att gat gag gaa cta gaa cgg gac aag agg gtc act tgg att            90            95            100            105            Lys Pro Pro Leu Tyr Met Gly Pro Gln Tyr Ile Lys Tyr Phe Asn Asp            339         </p>
	291	<p>           aaa ccc ccc cta tat atg ggc cct gag tat atc aag tac ttc aat gat            75            80            85            Ala Ile Val Met Met Lys Asn Arg Arg Ser Met Phe Leu Met Thr Cys            291         </p>
	243	<p>           gcc att gty atg aag aac cgc aga tcc atg ttc ctg atg acg tgc            60            65            70            Pro Cys Asp Phe Asp Trp Arg Gln Val Gln Ile Leu Met Phe Leu Ser            243         </p>
	195	<p>           ccg tgt gac ttt gac tgg aga gaa gty gag atc ctg atg ttt ctc agt            45            50            55            Leu Pro Pro Leu Cys His Gly Leu Pro Thr Gln Arg Gln Asp Gly Asn            195         </p>
		<p>           30            35            40         </p>

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 15 Lys Tyr Phe Lys Ser Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly  
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 60 65 70 75  
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 314 ctc ggc ctc acc ggc ctc tac ggc ttc atc ttc tac ctg ctc ggc tcc  
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 5 Tyr Cys Arg Thr Ser Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile  
 266 tat tgc cgg acc tgc gtg tca ggc ctg tgc ggg ggc acc ggc ggc atc  
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 218 Pro Phe Ile Ser Glu Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp  
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151	aag agc ctt ctg gtc ccc agt gcc ctc tcc ctc ctg ctc gcc ctc Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu	20	25	30	
199	ctc ctg cct cac tgc cag aag ctc ttt gtg tat gac ctt cac gca gtc Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val	35	40	45	
247	aag aac gac ttc cag att tgg agg tgc ata tgt gga aga ata tgc Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys	50	55	60	
295	ctt gat ctg aaa gat act ttc tgc agt agt ctg ctt att tat aat ttc Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe	65	70	75	80
343	agg ata ttt gaa aga ata gga agc aga aaa ttt gca tcc ttt tgc Arg Ile Phe Gln Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu	85	90	95	
391	ctg ggt tcc tgg gtt tgc tca gcc tta ttt gac ttt ctc ctc aat gaa Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Gln	100	105	110	
439	gct atg cag tat ttc ttc ggc atc act gca gct agt aat tgc cct tct Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser	115	120	125	
487	gga ttc ctg gca cct gtc ttt gct ctg ttt gta cca ttt tac tgc tcc Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser	130	135	140	
535	ata cca aga gtc caa gtc gca caa att ctg ggt ccg tgc tcc atc aca Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr	145	150	155	160
583	aac aag aca tgc att tat ata tgc gga ctg cag ctt ttc acc tct ggt Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly	165	170	175	
631	tcc tac atc tgg att gta gcc ata agt gga ctt atg tcc ggt ctg tgc Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys				
835	atg ttc acc agc acc ggc tcc agt ggg ctc tac aag gcg cct ctg tgc Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser	1	5	10	15
151	aag agc ctt ctg gtc ccc agt gcc ctc tcc ctc ctg ctc gcc ctc Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu	20	25	30	
199	ctc ctg cct cac tgc cag aag ctc ttt gtg tat gac ctt cac gca gtc Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val	35	40	45	
247	aag aac gac ttc cag att tgg agg tgc ata tgt gga aga ata tgc Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys	50	55	60	
295	ctt gat ctg aaa gat act ttc tgc agt agt ctg ctt att tat aat ttc Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe	65	70	75	80
343	agg ata ttt gaa aga ata gga agc aga aaa ttt gca tcc ttt tgc Arg Ile Phe Gln Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu	85	90	95	
391	ctg ggt tcc tgg gtt tgc tca gcc tta ttt gac ttt ctc ctc aat gaa Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Gln	100	105	110	
439	gct atg cag tat ttc ttc ggc atc act gca gct agt aat tgc cct tct Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser	115	120	125	
487	gga ttc ctg gca cct gtc ttt gct ctg ttt gta cca ttt tac tgc tcc Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser	130	135	140	
535	ata cca aga gtc caa gtc gca caa att ctg ggt ccg tgc tcc atc aca Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr	145	150	155	160
583	aac aag aca tgc att tat ata tgc gga ctg cag ctt ttc acc tct ggt Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly	165	170	175	
631	tcc tac atc tgg att gta gcc ata agt gga ctt atg tcc ggt ctg tgc Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys				

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	tac gac agc aaa atg ttc cag gtg cat cag gtg ctc tgc atc ccc agc	679		
	Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser			
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	Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser			
	210	215	220	
	tca gaa ccc acc agc gaa gcc aga att ggg atg gga gcc acg ctg gac	775		
	Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp			
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	Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe			
	245	250	255	
	tct cag ttt gca caa ggg agg cga cag aga cag cag gga gga atg	871		
15	Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Gly Met			
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	atc aat tgg aat cgt ctt ttt cct cct tta cgt cag cga caa aac gta	919		
	Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val			
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20	aac tat cag ggc ggt cgg cag tct gag cca gca gcg ccc cct cta gaa	967		
	Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu			
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	Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg			
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	Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val			
	325	330	335	
	gcc acc aac ttc ctg ctg cag cac tgatagtcac aggccaacac tgg	1110		
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	Thr Gly Val Asn Arg Thr Val Trp Glu Leu Ser Glu Glu Gly Val Tyr			
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	Gly Gln Asp Ser Pro Leu Glu Pro Val Ala Gly Val Leu Val Pro Pro			
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	gac ggg ccc ggg gcg ctt aac gcc tgt aac ccg cac acg aat ttc acg			519
	Asp Gly Pro Gly Ala Leu Asn Ala Cys Asn Pro His Thr Asn Phe Thr			
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	Ile Gln Arg Gly Gly Gly Cys Thr Phe Ala Asp Lys Ile His Leu Ala			
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20	tat gag aga ggg gcg tct gga gcc gtc atc ttt aac ttc ccc ggg acc			663
	Tyr Glu Arg Gly Ala Ser Gly Ala Val Ile Phe Asn Phe Pro Gly Thr			
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	Arg Asn Glu Val Ile Pro Met Ser His Pro Gly Ala Val Asp Ile Val			
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	gca atc atg atc ggc aat ctg aaa ggc aca aaa att ctg caa tct att			759
	Ala Ile Met Ile Gly Asn Leu Lys Gly Thr Lys Ile Leu Gln Ser Ile			
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30	360	370	380	Pro Leu Gln Gln His Val Gln Ser Thr Asn Gln Ser Leu Gln Val
				1383
25	345	350	355	Asn Gln Ile Ser Asn Ser Ala Ser Ser His Gln Gln Asp Asn Arg Ser
				1287
20	315	320	325	Arg Thr Cys Pro Met Cys Lys Cys Asp Ile Leu Lys Ala Leu Gly Ile
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15	280	285	290	Cys Ile Gln Leu Tyr Lys Pro Asn Asp Leu Val Arg Ile Leu Thr Cys
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(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
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(88) Date of publication of the international search report: 4 May 2000 (04.05.00)	

(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS

(57) Abstract

The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT, P 99/03929

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12N15/12 C07K14/705 C12N5/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	WO 98 21328 A (KATO SEISHI; PROTEGENE INC (JP); SEKINE SHINGO (JP); SAGAMI CHEM R) 22 May 1998 (1998-05-22) abstract page 17, last paragraph -page 18, paragraph 1	1-6
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X	DATABASE EMBLEMEST6 [online] Accession Number AI057511, 22 July 1998 (1998-07-22) STRAUSBERG R: "H. sapiens cDNA clone IMAGE:1653181 3' similar to SW:YJK4 yeast P42929 hypothetical 16.2 kD protein in SME1-MEF2 intergenic region" XP002123564 100% identity in 357 BP overlap with SEQ ID NO:11	1-6
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

Date of the actual completion of the international search

23 November 1999

Date of mailing of the international search report

0 6. 03. 00

Authorized officer

CUPIDO, M

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## INTERNATIONAL SEARCH REPORT

International Application No

PC JP 99/03929

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBLEST21 [Online]  Accession Number AA 482452,  24 June 1997 (1997-06-24)  HILLIER L ET AL.: "zv05b11.r1 Soares  NhHMPu S1 Homo sapiens cDNA clone 7527733  5'similar to SW:YJK4 yeast P42929  hypothetical 16.2 kD protein in SME1-MEF2  intergenic region"  XP002123565  99.7% identity in 367 BP overlap with SEQ  ID NO 11</p>	1-6
A	<p>---  D'ANDREA ET AL: "Molecular Cloning of  NKBl. A Natural Killer Cell Receptor for  HLA -B Allotypes"  JOURNAL OF IMMUNOLOGY,  vol. 155, no. 5,  1 September 1995 (1995-09-01), pages  2306-2310 2310, XP002111500  ISSN: 0022-1767  abstract  page 2307, right-hand column, line 16</p>	1-6
A	<p>---  GILLEN C M ET AL: "Molecular cloning and  functional expression of the K-C1  cotransporter from rabbit, rat, and  human."  JOURNAL OF BIOLOGICAL CHEMISTRY.,  vol. 271, no. 27,  5 July 1996 (1996-07-05), pages  16237-16244, XP002119528  AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS,  BALTIMORE, MD., US  ISSN: 0021-9258  abstract</p>	1-6
A	<p>---  KYTE J ET AL: "A SIMPLE METHOD FOR  DISPLAYING THE HYDROPATHIC CHARACTER OF A  PROTEIN"  JOURNAL OF MOLECULAR BIOLOGY,  vol. 157, no. 1, 5 May 1982 (1982-05-05),  pages 105-132, XP000609692  ISSN: 0022-2836  cited in the application  the whole document</p>	1-6
P,X	<p>---  DATABASE EMBLEST11 [Online]  Accession Number AI 553893,  25 March 1999 (1999-03-25)  STRAUSBERG R: "Homo sapiens cDNA clone  IMAGE:2169115 3'"  XP002123566  100% identity in 375 BP overlap with SEQ  ID 11</p> <p>-----</p>	1-6

In national application No.  
PCT/JP 99/03929

INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International Application, as follows:

see additional sheets

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-6 partially

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: Claims 1-6 partially

A protein comprising amino acid sequence SEQ ID NO 1, a DNA SEQ ID NO 11 or 21, encoding this protein, as well as an expression vector capable of expressing this sequence and a eukaryotic cell expressing the DNA

2. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 2 and DNA SEQ ID 12 and 22

3. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 3 and DNA SEQ ID 13 and 23

4. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 4 and DNA SEQ ID 14 and 24

5. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 5 and DNA SEQ ID 15 and 25

6. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 6 and DNA SEQ ID 16 and 36

7. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 7 and DNA SEQ ID 17 and 37

8. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 8 and DNA SEQ ID 18 and 38

9. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 9 and DNA SEQ ID 19 and 39

10. Claims: 1-6 partially  
Idem as subject 1 but limited to protein SEQ ID NO. 10 and  
DNA SEQ ID 20 and 30

11. Claims: 1-6 partially  
Idem as subject 1 but limited to protein SEQ ID NO. 31 and  
DNA SEQ ID 41 and 51

12. Claims: 1-6 partially  
Idem as subject 1 but limited to protein SEQ ID NO. 32 and  
DNA SEQ ID 42 and 52

13. Claims: 1-6 partially  
Idem as subject 1 but limited to protein SEQ ID NO. 33 and  
DNA SEQ ID 43 and 53

14. Claims: 1-6 partially  
Idem as subject 1 but limited to protein SEQ ID NO. 34 and  
DNA SEQ ID 44 and 54

15. Claims: 1-6 partially  
Idem as subject 1 but limited to protein SEQ ID NO. 35 and  
DNA SEQ ID 45 and 55

16. Claims: 1-6 partially  
Idem as subject 1 but limited to protein SEQ ID NO. 36 and  
DNA SEQ ID 46 and 56

17. Claims: 1-6 partially  
Idem as subject 1 but limited to protein SEQ ID NO. 37 and  
DNA SEQ ID 47 and 57

18. Claims: 1-6 partially  
Idem as subject 1 but limited to protein SEQ ID NO. 38 and  
DNA SEQ ID 48 and 58

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

19. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 39 and  
DNA SEQ ID 49 and 59

20. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 40 and  
DNA SEQ ID 50 and 60

21. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 61 and  
DNA SEQ ID 71 and 81

22. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 62 and  
DNA SEQ ID 72 and 82

23. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 63 and  
DNA SEQ ID 73 and 83

24. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 64 and  
DNA SEQ ID 74 and 84

25. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 65 and  
DNA SEQ ID 75 and 85

26. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 66 and  
DNA SEQ ID 76 and 86

27. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 67 and  
DNA SEQ ID 77 and 87

28. Claims: 1-6 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Idem as subject 1 but limited to protein SEQ ID NO. 68 and  
DNA SEQ ID 78 and 88

29. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 69 and  
DNA SEQ ID 79 and 89

30. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 70 and  
DNA SEQ ID 80 and 90

31. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 91 and  
DNA SEQ ID 101 and 111

32. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 92 and  
DNA SEQ ID 102 and 112

33. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 93 and  
DNA SEQ ID 103 and 113

34. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 94 and  
DNA SEQ ID 104 and 114

35. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 95 and  
DNA SEQ ID 105 and 115

36. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 96 and  
DNA SEQ ID 106 and 116

37. Claims: 1-6 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Idem as subject 1 but limited to protein SEQ ID NO. 97 and  
DNA SEQ ID 107 and 117

38. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 98 and  
DNA SEQ ID 108 and 118

39. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 99 and  
DNA SEQ ID 109 and 119

40. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 100 and  
DNA SEQ ID 110 and 120

41. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 121 and  
DNA SEQ ID 131 and 141

42. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 122 and  
DNA SEQ ID 132 and 142

43. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 123 and  
DNA SEQ ID 133 and 143

44. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 124 and  
DNA SEQ ID 134 and 144

45. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 125 and  
DNA SEQ ID 135 and 145

46. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 126 and

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

DNA SEQ ID 136 and 146

47. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 127 and  
DNA SEQ ID 137 and 147

48. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 128 and  
DNA SEQ ID 138 and 148

49. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 129 and  
DNA SEQ ID 139 and 149

50. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 130 and  
DNA SEQ ID 140 and 150

**Information on patent family members**

PC JP 99/03929

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9821328 A	22-05-1998	AU 4885297 A EP 0941320 A	03-06-1998 15-09-1999
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